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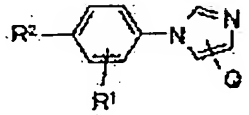
(71)Applicant : TAISHO PHARMACEUT CO LTD
(72)Inventor : SATO MASAKAZU
KAKINUMA HIROYUKI
UMEMIYA HIROKI
NAKAMURA TOSHIO

(54) IMIDAZOLE DERIVATIVE

(57)Abstract:
PROBLEM TO BE SOLVED: To obtain a medicine which inhibits 20-HETE-producing enzyme associated with microvascular constriction, dilation action, cell growth causing action, etc., in main organs such as the kidney, the cerebral blood vessel, etc.
SOLUTION: The 20-HETE-producing enzyme comprises an imidazole derivative represented by the formula [Q is a hydrogen atom or a 1-4C alkyl group; R1 is a hydrogen atom, a 1-6C alkyl group or a halogen atom; R2 is a 1-14C alkyl group, a 2-14C alkanoyl group, a morpholino group or a group represented by the formula: R3-O [R3 is a 1-14C alkyl group, a 2-14C alkenyl group, a 3-14C alkynyl group, a 3-10C cycloalkyl group, a 1-phenyl-2-propynyl group or a group represented by formula R4-A]] or its pharmaceutically permissible salt as an active ingredient.



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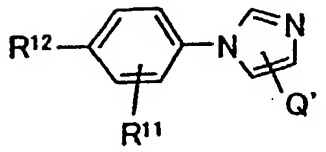
* NOTICES *

1.This document has been translated by computer. So the translation may not reflect the original precisely.
2.**** shows the word which can not be translated.
3.In the drawings, any words are not translated.

DETAILED DESCRIPTION

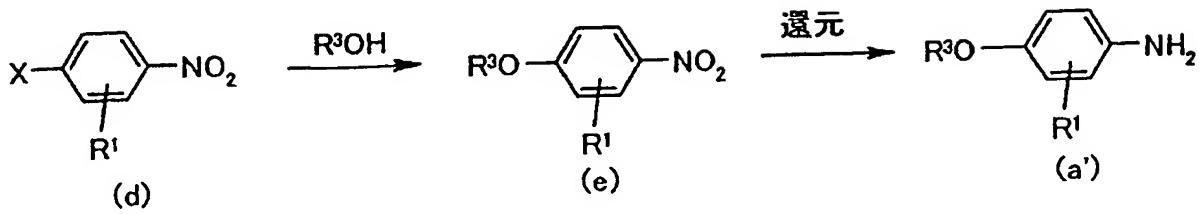
[Detailed Description of the Invention]
[0001]
[Field of the Invention]
This invention relates to the imidazole derivative which prevents the production enzyme of 20-hydroxyeicosatetraenoic acid (20-HETE) by which a biosynthesis is carried out from an arachidonic acid.
[0002]
[Description of the Prior Art]
The leukotrienes produced as a physiological active substance produced from an arachidonic acid by the prostagladins and RIPOKISHIGENAGE which are produced by cyclooxygenase are known widely. However, to carry out the work with 20-HETE variegated in the living body produced from an arachidonic acid with the enzyme belonging to cytochrome p450 group is being shown clearly in recent years. It is shown clearly until now that setting 20-HETE to main organs, such as the kidney and a cerebral blood vessel, and making a microvessel contracting or extending and cell proliferation are caused. While performing the important physiological function in the living body, various kidney disease, the cerebrovascular disease, participating in symptoms, such as cardiovascular disease, deeply is suggested (J.Vascular Research — the 79th page the 32nd volume in 1995) Am.J.Physiol., R of 277th volume 607 pages, 1999, Physiol.Rev., the 82nd volume, the 131st term, 2002.
[0003]
Moreover, many compounds of this invention and compounds which have similar structure are reported. For example, it is reported that the derivative whose R2 is a permutation C1 - C4 alkyl group has nit rucksack oxide synthetic enzyme inhibition activity in a formula (1) (International Patent Publication WO No. 9715555 specification). It is reported that the derivative whose R2 is a permutation alkanoyl radical has cranial nerve cell death depressor effect in a formula (1) (International Patent Publication WO No. 9418172 specification). Moreover, it is reported that the derivative whose R2 is a permutation phenylalkoxy radical is effective in preventing hyperlipemia or arteriosclerosis in a formula (1) (International Patent Publication WO No. 9529163 specification). And it is reported that the derivative whose R2 is a permutation alkoxy group is effective as anti-arrhythmia, preventing hypertension, or a high ischemia therapy agent in a formula (1) (the European Patent public presentation EP No. 0306440 specification, U.S. Pat. No. 5202346 number specification). However, having 20-HETE production enzyme ****** also in any is not reported.
[0004]
On the other hand, it is reported that an imidazolyl benzophenone derivative shows 20-HETE production enzyme ******, and ** cannot necessarily satisfy the (International Patent Publication WO No. 0168610 specification), activity, or physical properties.
[0005]
[Problem(s) to be Solved by the Invention]
This invention aims at offering the drugs which check production of 20-HETE which participates in the microvessel contraction in main organs, such as the kidney and a cerebral blood vessel, an



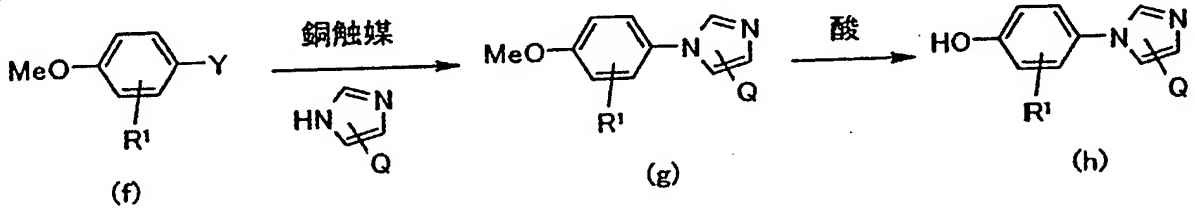
(2)

[0012]
Q' is a hydrogen atom, or C1 – C4 alkyl group among {type. R11 They are a hydrogen atom, C1 – C6 alkyl group, and a halogen atom. R12 R13 among a morpholino radical or a formula R13–O– [type C3 – C14 alkynyl group, C3 – C10 cycloalkyl radical, 1–phenyl–2–propynyl group, or formula R14–A' – (among a formula) R14 C3 – C10 cycloalkyl radical, C1 – C10 alkoxy group, C2 – C10 alkanoyl radical, a dioxoranyl group, the dioxoranyl group permuted by C1 – C6 alkyl group, An OKISANIRU radical, the dioxa nil radical, the dioxa nil radical permuted by C1 – C6 alkyl group, A benzodioxa nil radical, a bicyclo [2.2.1] heptane–2–IRU radical, C1 – C6 alkylthio group, a 4–C2 – C6 alkoxy carbonyl piperazine–1–IRU radical, it is pyrrolyl radical, N, and N–JI C1 – C6 alkylamino C1 – C6 alkoxy group, C1 C6 alkoxy [1] C – C6 alkoxy group, a furil radical, a thienyl group, and a pyrrolidone–1–IRU radical, and A' is C1 – C10 alkylene group. it is the radicai shown.] it is the radical come out of and shown. The imidazole derivative expressed with} or its salt permitted pharmaceutically is offered.
[0013]
Other this inventions offer the physic which makes an active principle the above–mentioned imidazole derivative or its salt permitted pharmaceutically.
Other this inventions offer the kidney disease, cerebrovascular disease, or cardiovascular disease remedy which makes an active principle the above–mentioned imidazole derivative or its salt permitted pharmaceutically.
[0014]
The vocabulary used in this invention is defined below.
In this invention, "Cx–Cy" shows that the radical which continues after that has the carbon atom of a x–y individual.
[0015]
A halogen atom is a fluorine atom, a chlorine atom, a bromine atom, or an iodine atom, is a fluorine atom, a chlorine atom, or a bromine atom preferably, and is a fluorine atom or a chlorine atom more preferably.
C1 – C14 alkyl group mean the alkyl group of the shape of the shape of a straight chain which has 1–14 carbon atoms, and branching, and C1 – its C8 alkyl group are desirable. As C1 – C8 alkyl group, methyl group, ethyl group, n–propyl group, n–butyl, n–hexyl group, n–heptyl radical, n–octyl radical, isobutyl radical, sec–butyl, isopentyl radical, iso hexyl group, 3–methyl heptyl radical, 3, and 3–dimethyl butyl etc. is more desirable, for example.
C3 – C10 cycloalkyl radical mean the annular alkyl group which has 3–10 carbon atoms, for example, a cyclo propyl group, cyclo butyl, a cyclopentylic group, a cyclohexyl radical, a cycloheptyl radical, a cyclo octyl radical, etc. are mentioned. Especially, a cyclo propyl group, a cyclopentylic group, and a cyclohexyl radical are desirable.
[0016]
C2 – C14 alkenyl radical mean the alkenyl radical of the shape of the shape of a straight chain which has at least one double bond and 2–14 carbon atoms, and branching. For example, an ethenyl radical, a propenyl radical, 2–butenyl group, a 3–methyl–2–butenyl group, A pentenyl radical, a 2–methyl–2–pentenyl radical, a hexenyl radical, 2, 4–hexa dienyl radical, a heptenyl radical, an octenyl group, 3, the 7–dimethyl –2, 6–OKUTA dienyl radical, etc. are mentioned.
C2 – C14 alkynyl group mean the alkynyl group of the shape of the shape of a straight chain which has at least one triple bond and 2–6 carbon atoms, and branching, for example, an ethynyl group, 2–propynyl group, a butynyl radical, 5–cutting–pliers nil radical, a hexenyl radical, a

more preferably permuted by the methyl group, for example, a 4-methyl thiazole-5-IRU radical etc. is mentioned.
A pyridyl radical contains 2-pyridyl radical, 3-pyridyl radical, and 4-pyridyl radical. A pyrrolyl radical has desirable 1-pyrrolyl radical (N-pyrrolyl radical) including 1-pyrrolyl radical, 2-pyrrolyl radical, and 3-pyrrolyl radical.
[0023]
N and N-JI C1 - C6 alkylamino C1 - C6 alkoxy group have the gestalt which N and N-JI C1 - C6 alkylamino radical, and C1 - C6 alkoxy group compounded, and N and N-diethylaminoethoxy radical etc. is mentioned.
A pyrrolidone-1-IRU radical contains a 2-pyrrolidone-1-IRU radical and a 3-pyrrolidone-1-IRU radical.
[0024]
C1 defined by A and A' - C10 alkylene group mean the alkylene group of the shape of the shape of a straight chain which has 1-10 carbon atoms, and branching, for example, methylene group, methyl methylene group, ethylene, propylene radical, heptylene radical, 2, and 2-dimethyl propylene radical, a hexylene radical, etc. are mentioned.
[0025]
Various kinds of above-mentioned radicals and besides the permuted gestalt which was mentioned above At least one hydrogen atom on the radical For example, a fluorine atom, a chlorine atom, Halogen atom; nitro group; amino-group; hydroxy group; thiol group; formyl group; carboxyl group; cyano group; carbamoyl groups, such as a bromine atom and an iodine atom; A methyl group, An ethyl group, a propyl group, an isopropyl group, butyl, an isobutyl radical, sec-butyl, tert-butyl, a pentyl radical, an isopentyl radical, Alkyl groups, such as a neopentyl radical and a tert-pentyl radical; A phenyl group, Aryl groups, such as a naphthyl group, a biphenyl radical, and an anthranil; A pyrrolyl radical, Alkoxy carbonyl groups, such as heterocycle radical; methoxycarbonyl groups, such as a pyridyl radical and a thienyl group, and an ethoxycarbonyl radical; An acetyl group, Acyl groups, such as benzoyl; a non-hydrogen atom or radicals, such as alkoxy group; methylthio radicals, such as a methoxy group, an ethoxy radical, and a propoxy group, an ethyl thio radical, and a propyl thio radical, may permute. [, such as alkylthio group;,] In addition, the carbon atomic number in these substituents is not contained in above-mentioned x or y.
[0026]
With the salt permitted pharmaceutically, moreover, alkaline metals and alkaline earth metal, It is a salt with a salt with ammonium, alkylammonium, etc., a mineral acid, or an organic acid. For example, sodium salt, potassium salt, a calcium salt, ammonium salt, An aluminum salt, triethyl ammonium salt, acetate, propionate, Butyrate, a formic acid salt, a trifluoroacetic acid salt, a maleate, a tartrate, citrate, A stearate, succinate, ethyl succinate, a salt lactobionate, Gluconate, glucoheptonate, a benzoate, a methansulfonic acid salt, An ethane-sulfonic-acid salt, a 2-hydroxy ethane-sulfonic-acid salt, a benzenesulfonic acid salt, A Para toluenesulfonic acid salt, a lauryl sulfate, malate, an aspartic-acid salt, Glutamate, adipate, a salt with a cysteine, a salt with N-acetylcysteine, A hydrochloride, the hydrobromate, phosphate, a sulfate, an iodine hydro acid salt, a nicotinic-acid salt, an oxalate, a picrate, a thiocyanate, an undecanoic acid salt, a salt with an acrylic-acid polymer, a salt with a carboxyvinyl polymer, etc. can be mentioned.
[0027]
[Embodiment of the Invention]
this invention compound (1) is compoundable by the approach shown below.
[0028]
[Formula 5]



[0033]
Manufacturing method 3; it is the following, and the aniline derivative (a') (R2 shows a permutation alkoxy group, i.e., R2=R3O) which is synthetic intermediate field can be made and compounded. Namely, a nitrobenzene derivative (d) (leaving groups, such as a fluorine and chlorine, are shown by the inside X of a formula) other notations -- the above -- being synonymous -- the inside of a suitable solvent (a methanol and ethanol --) Propanol, a tetrahydrofuran, dioxane, toluene, a methylene chloride, Chloroform, an acetonitrile, ethyl acetate, dimethyl sulfoxide, need, such as dimethylformamide, -- responding -- a base (triethylamine, N, and N-diisopropyl ethylamine --) It can react with various corresponding alcohols under existence of a pyridine, potassium carbonate, a calcium carbonate, cesium carbonate, sodium hydride, sodium methoxide, a t-butoxy potassium, etc., and a compound (e) can be manufactured. At this time, 0 degree C - 80 degrees C of reaction temperature are 0 degree C - a room temperature preferably, and reaction time is 1 - 2 hours preferably for 1 to 12 hours. next, a compound (e) -- the inside of a suitable solvent (a methanol, ethanol, and propanol --) A tetrahydrofuran, dioxane, toluene, a methylene chloride, chloroform, Reducing agents, such as an acetonitrile and ethyl acetate (under palladium activated carbon / hydrogen ambient atmosphere) Palladium activated carbon / hydrazine hydrate, palladium activated carbon / ammonium formate, Tin(II) chloride 1 hydrate, iron/ammonium chloride, a Raney nickel catalyst / hydrazine hydrate, etc. can manufacture an aniline derivative (a') by returning a nitro group using the bottom of palladium activated carbon / hydrogen ambient atmosphere preferably. reaction temperature -- room temperature - it is room temperature -100 degree C preferably, and 150 degrees C of reaction time are 1 hour - 24 hours.
[0034]
[Formula 8]

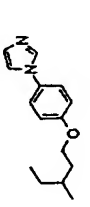
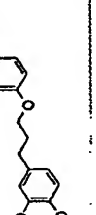
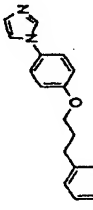
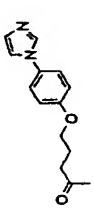
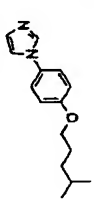
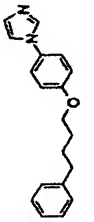
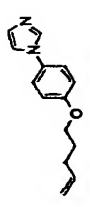


[0035]
Manufacturing method 4; through intermediate field (h), a compound (1) is the following, and can be made and manufactured. A phenyl boron acid or a halogenation phenyl derivative (f) (the inside Y of a formula expresses B(OH)2 or a halogen atom) other notations -- the above -- being synonymous -- the inside of a suitable solvent (a methanol and ethanol --) Propanol, a tetrahydrofuran, dioxane, toluene, a methylene chloride, Chloroform, an acetonitrile, ethyl acetate, dimethyl sulfoxide, By dimethylformamide etc., under copper catalyst ([Cu(OH) TMEDA] 2Cl2, 2b(CuOTf) enzene, etc.) existence, It condenses with an imidazole derivative under an oxygen ambient atmosphere preferably, and intermediate field (g) can be manufactured [Organic Lett., the 2nd volume, and the 1237th term (2000)]. The room temperature of reaction temperature is desirable and reaction time is 12 - 24 hours. Subsequently, intermediate field (g) can be reacted at 100 degrees C - 150 degrees C among 48% hydrogen bromide, and an

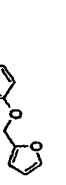
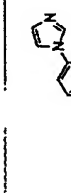
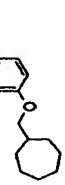
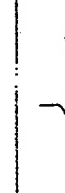
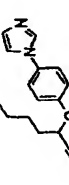
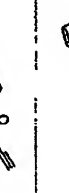
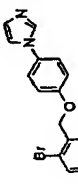
disease, the cerebrovascular disease, and various cardiovascular disease remedies.
[0041]
[Example]
Hereafter, an example is given and this invention is explained in more detail.
Example 1
Manufacture of a 1-[4-propyl phenyl]-imidazole hydrochloric acid (compound 108)
4-propyl aniline (2.03g, 0.0150 mols) Triethyl orthoformate (4.99g, 0.337 mols) Mixture was stirred at 100 degrees C for 7 hours. After cooling to a room temperature, it is a methanol to reaction mixture. (15mL) The amino acetaldehyde dimethyl acetal (5.69g, 0.0541 mols) was added, and it stirred at the room temperature for 30 minutes, and stirred at 100 more degrees C for 4 hours. They are dimethoxyethane (20mL) and a 1M titanium-tetrachloride-toluene solution to the residue which condensed reaction mixture and was obtained after cooling to a room temperature. (21mL, 0.021 mols) In addition, it stirred under heating reflux further at the room temperature for 4 hours for 1 hour. After cooling to a room temperature, the sodium-hydroxide water solution was added to reaction mixture, and chloroform extracted. The organic layer was dried and condensed with magnesium sulfate. A silica gel chromatography (chloroform-methanol = 97:3) refines the obtained residue, and it is a 1-[4-propyl phenyl]-imidazole. (2.0g) It obtained as brown oily matter. A 4-N hydrochloric-acid-ethyl-acetate solution is added to a product, and it recrystallizes [mixed solvent / of ethyl-acetate-chloroform], and is an end of non-color powder-like title compound. (1.38g, 41.2%) It obtained. The 155.5 to 157.0 degree C melting point
[0042]
Example 2
Manufacture of [2-[2-(4-imidazole-1-IRU-phenoxy)-ethoxy]-ethyl]-dimethylamine 2 hydrochloric acid (compound 116)
Sodium hydride (60% oil, 1.0 g, 0.26 mols) Dimethylformamide (3.0ml) Bottom of ice-cooling to suspension, N, and N-dimethylamino ethyloxy ethanol (2.3g, 0.26 mols) Dimethylformamide solution (5ml) It was dropped and stirred for 10 minutes. It is 4-fluoro nitrobenzene to this reaction mixture. (3g, 0.021 mols) Dimethylformamide solution (10mL) It was dropped and stirred at the room temperature for 2 hours. Water is added to a reaction mixture, ethyl acetate extracts, after saturation brine washing, it dries MgSO4, an organic layer is condensed under reduced pressure, and it is a dimethyl-[2-[2-(4-nitro phenoxy)-ethoxy]-ethyl] amine. (5.9g) It obtained. It is a methanol about the compound obtained above. (100mL) It dissolves and is 10% palladium activated carbon. (0.6g) In addition, it stirred at the room temperature under the hydrogen ambient atmosphere for 3 hours. After checking disappearance of a raw material by TLC analysis, cerite is used, insoluble matter is filtered, filtrate is condensed, and it is an aniline derivative. (5.0g) It obtained as brown oily matter. Next, it is a triethyl orthoformate to this aniline derivative. (10mL, 0.060 mols) In addition, it stirred at 100 degrees C for 20 hours. After cooling to a room temperature, they are a methanol (80mL) and an amino acetaldehyde dimethyl acetal to reaction mixture. (6.8mL, 0.063 mols) In addition, it stirred at 100 degrees C for 1.5 hours. It is dimethoxyethane to the residue which condensed reaction mixture and was obtained. (30mL) 1M titanium-tetrachloride-toluene solution (25mL, 0.025 mols) In addition, it stirred under heating reflux for 5 hours. After cooling to a room temperature, the sodium-hydroxide water solution was added to reaction mixture. After filtering the insoluble matter which deposited, ethyl acetate extracted filtrate. The organic layer was dried and condensed with magnesium sulfate after saturation brine washing. NH mold silica gel chromatography (hexane-ethyl acetate = 1:2) refines the obtained residue. [2-[2-(4-imidazole-1-IRU-phenoxy)-ethoxy]-ethyl]-dimethylamine (0.40g, 6.9%) was obtained as oily matter. The product was dissolved in the ether, the powder which added the 4M hydrochloric-acid-ethyl-acetate solution, condensed, and deposited was washed with ethyl acetate, and the title compound was obtained. (428mg) . The 174.0 to 179.0 degree C melting point
[0043]
Example 3
Manufacture of 1-[4-propyloxy phenyl]-imidazole toluenesulfonate (compound 94)
4-(imidazole-1-IRU) phenol (1.0g, 6.25mmol) Propanol (563mg, 9.38mmol) Triphenyl phosphine

化合物番号	構造式	^{1}H NMR (300MHz, $CDCl_3$) spectra and melting points	抑制率 % at 0.1uM	IC_{50} (nM)
化合物 1		δ 1.86-2.04 (m, 4H), 2.15 (m, 2H), 2.79 (m, 1H), 3.96 (d, J = 6.7Hz, 2H), 6.98 (m, J_{AB} = 8.9Hz, 2H), 7.18 (s, 1H), 7.20 (s, 1H), 7.29 (m, J_{AB} = 8.9Hz, 2H), 7.76 (s, 1H).	85.8	
化合物 2		δ 1.03-1.22 (m, 4H), 1.27 (d, J = 6.1Hz, 3H), 1.58-1.80 (m, 6H), 1.93 (m, 1H), 4.15 (d, J = 6.1Hz, 1H), 6.95 (m, J_{AB} = 9.0Hz, 2H), 7.18 (s, 1H), 7.20 (s, 1H), 7.28 (m, J_{AB} = 9.0Hz, 2H), 7.76 (s, 1H).	79.6	
化合物 3		δ 1.04-1.19 (m, 2H), 1.20-1.39 (m, 3H), 1.62-1.92 (m, 6H), 3.78 (d, J = 6.2Hz, 2H), 6.96 (m, J_{AB} = 8.9Hz, 2H), 7.18 (s, 1H), 7.20 (s, 1H), 7.28 (m, J_{AB} = 8.9Hz, 2H), 7.76 (s, 1H).	84.4	
化合物 4		δ 1.00 (m, 2H), 1.19-1.38 (m, 3H), 1.45-1.80 (m, 8H), 4.03 (t, J = 6.7Hz, 2H), 6.98 (m, J_{AB} = 8.9Hz, 2H), 7.18 (s, 1H), 7.20 (s, 1H), 7.28 (m, J_{AB} = 8.9Hz, 2H), 7.76 (s, 1H).	94.1	
化合物 5		δ 4.37 (s, 4H), 6.95-6.98 (m, 3H), 7.05 (m, J_{AB} = 8.9Hz, 2H), 7.19 (s, 1H), 7.22 (s, 1H), 7.26-7.33 (m, 3H), 7.77 (s, 1H).	96.9	
化合物 6		δ 3.14 (t, J = 7.5Hz, 2H), 3.86 (s, 3H), 4.19 (t, J = 7.5Hz, 2H), 6.88-6.95 (m, 2H), 6.99 (m, J_{AB} = 8.9Hz, 2H), 7.18-7.13 (m, 6H), 7.76 (s, 1H).	97.3	
化合物 7		δ 3.07 (t, J = 6.7Hz, 2H), 4.18 (t, J = 6.7Hz, 2H), 6.96 (m, J_{AB} = 9.0Hz, 2H), 7.16-7.20 (m, 4H), 7.29 (m, J_{AB} = 9.0Hz, 2H), 7.45 (m, J_{AB} = 8.2Hz, 2H), 7.75 (s, 1H).	100.8	

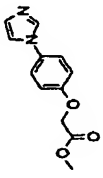
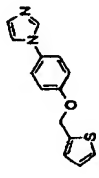
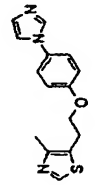
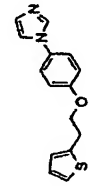
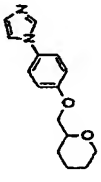
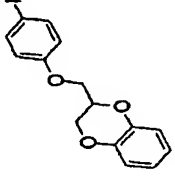
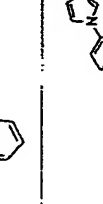
[0049]
[Table 2]

化合物 15		δ 0.92 (d, J = 7.5Hz, 3H), 0.96 (d, J = 6.4Hz, 3H), 1.26 (m, 1H), 1.40 (m, 1H), 1.62 (m, 2H), 1.84 (m, 1H), 4.02 (m, 2H), 6.97 (m, J_{AB} = 8.9Hz, 2H), 7.18 (s, 1H), 7.20 (s, 1H), 7.29 (m, J_{AB} = 8.9Hz, 2H), 7.76 (s, 1H).	104.0
化合物 16		δ 2.11 (tt, J = 6.2, 7.2Hz, 2H), 2.78 (t, J = 7.2Hz, 2H), 3.84 (s, 3H), 3.87 (s, 3H), 3.99 (t, J = 6.2Hz, 2H), 6.74-6.82 (m, 3H), 6.85 (m, J_{AB} = 9.0Hz, 2H), 7.19 (s, 1H), 7.20 (s, 1H), 7.29 (m, J_{AB} = 9.0Hz, 2H), 7.76 (s, 1H).	97.4
化合物 17		δ 2.10 (tt, J = 6.4, 7.2Hz, 2H), 2.77 (t, J = 7.2Hz, 2H), 3.78 (s, 3H), 3.98 (t, J = 6.4Hz, 2H), 6.85 (m, J_{AB} = 8.5Hz, 2H), 6.96 (m, J_{AB} = 9.0Hz, 2H), 7.13 (m, J_{AB} = 8.5Hz, 2H), 7.18 (s, 1H), 7.20 (s, 1H), 7.29 (m, J_{AB} = 9.0Hz, 2H), 7.76 (s, 1H).	99.5
化合物 18		δ 2.09 (tt, J = 6.1, 7.2Hz, 2H), 2.19 (s, 3H), 2.68 (t, J = 7.2Hz, 2H), 4.02 (t, J = 6.1Hz, 2H), 6.96 (m, J_{AB} = 9.0Hz, 2H), 7.18 (s, 1H), 7.20 (s, 1H), 7.29 (m, J_{AB} = 9.0Hz, 2H), 7.76 (s, 1H).	105.4
化合物 19		δ 0.94 (d, J = 6.5Hz, 6H), 1.37 (m, 2H), 1.63 (m, 2H), 1.81 (m, 2H), 3.98 (t, J = 6.5Hz, 2H), 6.98 (m, J_{AB} = 8.8Hz, 2H), 7.18 (s, 1H), 7.20 (s, 1H), 7.29 (m, J_{AB} = 8.8Hz, 2H), 7.76 (s, 1H).	85.7
化合物 20		δ 1.80-1.90 (m, 4H), 2.71 (t, J = 7.1Hz, 2H), 4.00 (t, J = 6.1Hz, 2H), 6.95 (m, J_{AB} = 9.0Hz, 2H), 7.18-7.32 (m, 9H), 7.76 (s, 1H).	94.0
化合物 21		δ 1.91 (m, 2H), 2.25 (m, 2H), 4.01 (t, J = 6.4Hz, 2H), 5.01-5.12 (m, 2H), 5.85 (m, 1H), 6.98 (m, J_{AB} = 8.9Hz, 2H), 7.18 (s, 1H), 7.20 (s, 1H), 7.29 (m, J_{AB} = 8.9Hz, 2H), 7.76 (s, 1H).	99.2

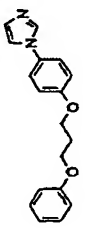
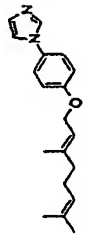
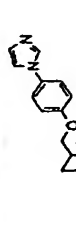
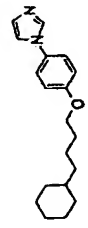
[0051]
[Table 4]

化合物 29		δ 5.05 (s, 2H), 6.40 (dd, J = 1.9, 3.1Hz, 1H), 6.47 (d, J = 3.1Hz, 1H), 7.07 (m, J_{AB} = 9.0Hz, 2H), 7.19 (s, 1H), 7.21 (s, 1H), 7.31 (m, J_{AB} = 9.0Hz, 2H), 7.48 (d, J = 1.9Hz, 1H), 7.77 (s, 1H).	64.1
化合物 30		δ 1.26-2.03 (m, 13H), 3.76 (d, J = 6.5Hz, 2H), 6.97 (m, J_{AB} = 8.9Hz, 2H), 7.18 (s, 1H), 7.20 (s, 1H), 7.28 (m, J_{AB} = 8.9Hz, 2H), 7.76 (s, 1H).	102.2
化合物 31		δ 0.92 (t, J = 7.0Hz, 3H), 1.26-1.39 (m, 4H), 1.59 (m, 2H), 1.97 (m, 2H), 4.74 (m, 1H), 7.11 (m, J_{AB} = 9.0Hz, 2H), 7.19 (s, 1H), 7.21 (s, 1H), 7.31 (m, J_{AB} = 9.0Hz, 2H), 7.77 (s, 1H).	87.1
化合物 32		δ 5.18 (s, 2H), 7.07 (m, J_{AB} = 8.9Hz, 2H), 7.19 (s, 1H), 7.21 (s, 1H), 7.26 (m, 1H), 7.32 (m, J_{AB} = 8.9Hz, 2H), 7.36 (m, 1H), 7.74 (d, J = 7.6Hz, 1H), 7.60 (d, J = 7.9Hz, 1H), 7.77 (s, 1H).	108.3
化合物 33		δ 5.17 (s, 2H), 7.05 (m, J_{AB} = 8.9Hz, 2H), 7.19 (s, 1H), 7.21 (s, 1H), 7.26-7.35 (m, 3H), 7.45-7.52 (m, 2H), 7.77 (s, 1H).	106.6
化合物 34		δ 3.88 (s, 3H), 5.16 (s, 2H), 6.93 (d, J = 8.4Hz, 1H), 6.99 (d, J = 7.3Hz, 1H), 7.07 (m, J_{AB} = 8.9Hz, 2H), 7.18 (s, 1H), 7.20 (s, 1H), 7.26-7.35 (m, 3H), 7.44 (d, J = 7.3Hz, 1H), 7.76 (s, 1H).	108.9
化合物 35		δ 3.90 (s, 6H), 5.16 (s, 2H), 6.93 (dd, J = 2.3, 7.5Hz, 1H), 7.04-7.13 (m, 4H), 7.18 (s, 1H), 7.20 (s, 1H), 7.30 (m, J_{AB} = 8.9Hz, 2H), 7.76 (s, 1H).	97.2

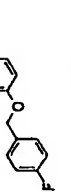
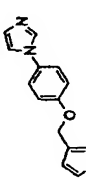
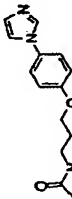
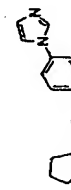
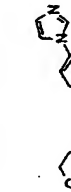
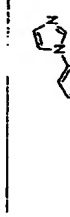
[0053]
[Table 6]

化合物 43		δ 3.83 (s, 3H), 4.69 (s, 2H), 7.00 (m, J_{AB} = 9.0Hz, 2H), 7.19 (s, 1H), 7.21 (s, 1H), 7.32 (m, J_{AB} = 9.0Hz, 2H), 7.78 (s, 1H).	61.3
化合物 44		δ 5.27 (s, 2H), 7.02 (m, 1H), 7.07 (m, J_{AB} = 8.9Hz, 2H), 7.14 (d, J = 3.4Hz, 1H), 7.19 (s, 1H), 7.21 (s, 1H), 7.31 (m, J_{AB} = 8.9Hz, 2H), 7.35 (m, 1H), 7.77 (s, 1H).	99.7
化合物 45		δ 2.47 (s, 3H), 3.28 (t, J = 6.4Hz, 2H), 4.18 (t, J = 6.4Hz, 2H), 6.98 (m, J_{AB} = 9.0Hz, 2H), 7.19 (s, 1H), 7.20 (s, 1H), 7.30 (m, J_{AB} = 9.0Hz, 2H), 7.76 (s, 1H), 8.61 (s, 1H).	96.0
化合物 46		δ 3.34 (t, J = 6.7Hz, 2H), 4.23 (t, J = 6.7Hz, 2H), 5.95 (m, 1H), 7.00 (m, J_{AB} = 8.9Hz, 2H), 7.18 (s, 1H), 7.19 (m, 1H), 7.20 (s, 1H), 7.29 (m, J_{AB} = 8.9Hz, 2H), 7.76 (s, 1H).	100.4
化合物 47		δ 1.45-1.76 (m, 6H), 3.53 (m, 1H), 3.74 (m, 1H), 3.92 (dd, J = 3.9, 10.0Hz, 1H), 4.00 (dd, J = 6.4, 10.0Hz, 1H), 4.08 (m, 1H), 7.01 (m, J_{AB} = 8.9Hz, 2H), 7.18 (s, 1H), 7.20 (s, 1H), 7.29 (m, J_{AB} = 8.9Hz, 2H), 7.76 (s, 1H).	10.9
化合物 48		δ 4.17-4.30 (m, 3H), 4.42 (dd, J = 2.5, 11.4Hz, 1H), 4.59 (m, 1H), 6.86-6.95 (m, 4H), 7.03 (m, J_{AB} = 8.9Hz, 2H), 7.19 (s, 1H), 7.21 (s, 1H), 7.28 (m, J_{AB} = 8.9Hz, 2H), 7.77 (s, 1H).	15.1
化合物 49		δ 2.50 (s, 3H), 5.08 (s, 2H), 7.04 (m, J_{AB} = 8.9Hz, 2H), 7.19 (s, 1H), 7.21 (s, 1H), 7.26-7.38 (m, 6H), 7.76 (s, 1H).	95.0

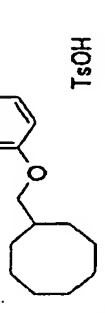
[0055]
[Table 8]

化合物 57		δ 2.29 (quint, J = 6.0Hz, 2H), 4.18 (t, J = 6.1Hz, 2H), 4.21 (t, J = 6.1Hz, 2H), 6.91-7.02 (m, 5H), 7.18 (s, 1H), 7.20 (s, 1H), 7.26-7.33 (m, 4H), 7.76 (s, 1H).	98.0
化合物 58		δ 1.61 (s, 3H), 1.76 (s, 3H), 1.82 (s, 3H), 2.08-2.17 (m, 4H), 4.58 (d, J = 6.7Hz, 2H), 5.09 (m, 1H), 5.49 (t, J = 6.7Hz, 1H), 6.99 (m, J_{AB} = 8.8Hz, 2H), 7.19 (s, 1H), 7.21 (s, 1H), 7.29 (m, J_{AB} = 8.8Hz, 2H), 7.77 (s, 1H).	100.7
化合物 59		δ 1.13-1.82 (m, 9H), 2.28-2.62 (m, 2H), 3.85-4.00 & 3.28-3.69 (m, 2H), 6.99 (m, J_{AB} = 9.0Hz, 2H), 7.19 (s, 1H), 7.20 (s, 1H), 7.29 (m, J_{AB} = 9.0Hz, 2H), 7.76 (s, 1H).	96.1
化合物 60		δ 0.87-0.94 (m, 2H), 1.08-1.33 (m, 6H), 1.43-1.53 (m, 2H), 1.63-1.83 (m, 7H), 3.98 (t, J = 6.5 Hz, 2H), 6.97 (m, J_{AB} = 9.0Hz, 2H), 7.18 (s, 1H), 7.20 (s, 1H), 7.29 (m, J_{AB} = 9.0Hz, 2H), 7.76 (s, 1H).	58.8
化合物 61		δ 0.74 (s, 3H), 1.21 (s, 3H), 2.15 (dt, J = 5.1, 6.5Hz, 2H), 3.46 (d, J = 11.0Hz, 2H), 3.63 (d, J = 11.0Hz, 2H), 4.14 (t, J = 6.5Hz, 2H), 4.70 (t, J = 5.1Hz, 1H), 6.99 (m, J_{AB} = 8.8Hz, 2H), 7.19 (s, 1H), 7.20 (s, 1H), 7.29 (m, J_{AB} = 8.8Hz, 2H), 7.76 (s, 1H).	91.8
化合物 62		δ 1.26 (t, J = 7.1Hz, 3H), 1.45-1.58 (m, 2H), 1.65-1.75 (m, 2H), 1.77-1.88 (m, 2H), 2.35 (t, J = 7.4Hz, 2H), 3.99 (t, J = 6.4Hz, 2H), 4.14 (q, J = 7.1Hz, 2H), 6.97 (m, J_{AB} = 8.8Hz, 2H), 7.18 (s, 1H), 7.20 (s, 1H), 7.29 (m, J_{AB} = 8.8Hz, 2H), 7.76 (s, 1H).	98.0
化合物 63		δ 3.09 (t, J = 6.8Hz, 2H), 4.20 (t, J = 6.8Hz, 2H), 6.97 (m, J_{AB} = 8.8Hz, 2H), 7.17-7.32 (m, 5H), 7.39 (ddd, J = 1.7, 2.1, 7.1Hz, 1H), 7.45 (d, J = 1.7Hz, 1H), 7.76 (s, 1H).	92.9

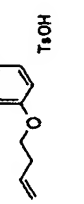
[0057]
[Table 10]

化合物 71		δ 5.07 (s, 2H), 7.03-7.46 (m, 10H), 7.77 (s, 1H). mp 91.5-93.0℃	109.0	1.3	
化合物 72		δ 4.99 (s, 2H), 6.51 (d, J = 1.1Hz, 1H), 7.01-7.09 (m, 2H), 7.19-7.36 (m, 4H), 7.46 (t, J = 1.7Hz, 1H), 7.54 (dd, J = 0.9, 1.7Hz, 1H), 7.78 (t, J = 1.1Hz, 1H). mp 114.5-115.5℃	99.3	4.7	
化合物 73		δ 2.01-2.13 (m, 4H), 2.40 (t, J = 8.4Hz, 2H), 3.38-3.54 (m, 4H), 4.03 (t, J = 6.2Hz, 2H), 6.97 (m, J_{AB} = 8.8Hz, 2H), 7.18 (s, 1H), 7.20 (s, 1H), 7.29 (m, J_{AB} = 8.8Hz, 2H), 7.76 (s, 1H).	72.4	7.3	
化合物 74		δ 2.58-2.67 (m, 4H), 2.84 (t, J = 5.7Hz, 2H), 3.71-3.78 (m, 4H), 4.15 (t, J = 5.7Hz, 2H), 6.97 (m, J_{AB} = 8.8Hz, 2H), 7.18 (s, 1H), 7.20 (s, 1H), 7.29 (m, J_{AB} = 8.8Hz, 2H), 7.76 (s, 1H).	55.2	33.5	
化合物 75		δ 2.60 (m, 4H), 2.83 (t, J = 5.6Hz, 2H), 3.75 (m, 4H), 4.15 (t, J = 5.6Hz, 2H), 7.00 (m, J_{AB} = 8.9Hz, 2H), 7.19 (s, 1H), 7.20 (s, 1H), 7.30 (m, J_{AB} = 8.9Hz, 2H), 7.76 (s, 1H). mp 41.0-43.5℃	66.7	8.6	
化合物 76		(200 MHz, *DMSO-d_6*) δ 5.24 (s, 2H), 7.08 (t, J = 1.1Hz, 2H), 7.10-7.21 (m, 2H), 7.37 (m, 1H), 7.50-7.63 (m, 3H), 7.65 (t, J = 1.3Hz, 1H), 7.78 (dt, J = 1.8, 7.7Hz, 1H), 8.14 (t, J = 1.1Hz, 1H), 8.60 (m, 1H). mp 94.0-95.0℃	70.8	4.5	
化合物 77		δ 5.14 (s, 2H), 7.07 (m, J_{AB} = 8.8Hz, 2H), 7.18 (s, 1H), 7.20 (s, 1H), 7.27-7.79 (m, 3H), 7.78-7.83 (m, 2H), 8.63 (dd, J = 1.8, 4.8Hz, 1H), 8.72 (d, J = 2.2Hz, 1H). mp 117.5-119.0℃	93.7	0.63	

[0059]
[Table 12]

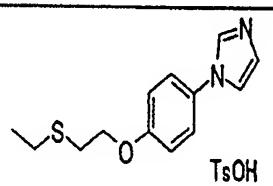
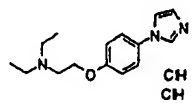
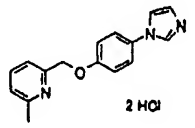
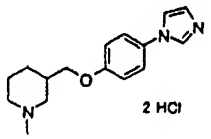
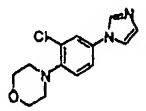
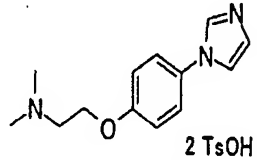
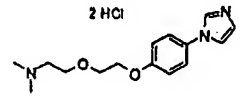
化合物 85		(200 MHz, *DMSO-d_6*), δ 1.28–2.15 (m, 15H), 2.29 (s, 3H), 3.84 (d, *J* = 6.6Hz, 2H), 7.08–7.25 (m, 4H), 7.48 (m, J_{AB} =8.1Hz, 2H), 7.70 (m, J_{AB} = 9.0Hz, 2H), 7.89 (dd, *J* = 1.5, 1.8Hz, 1H), 8.21 (dd, *J* = 1.3, 1.8Hz, 1H), 9.56 (dd, *J* = 1.3, 1.5Hz, 1H). mp 232.5–233.0℃	91.6	2.7
化合物 86		(200 MHz, *DMSO-d_6*) δ 1.10 (s, 3H), 1.13 (s, 3H), 2.29 (s, 3H), 3.55–3.78 (m, 3H), 4.13–4.20 (m, 2H), 7.11 (m, J_{AB} = 7.9Hz, 2H), 7.20 (m, J_{AB} = 9.2Hz, 2H), 7.48 (m, J_{AB} =8.1Hz, 2H), 7.72 (m, J_{AB} = 9.0Hz, 2H), 7.89 (dd, *J* = 1.5, 1.8Hz, 1H), 8.22 (dd, *J* = 1.3, 1.8Hz, 1H), 9.58 (dd, *J* = 1.3, 1.5Hz, 1H). mp 150.0–153.0℃	90.0	5.5
化合物 87		*DMSO-d_6*, δ 2.29 (s, 3H), 3.25 (s, 3H), 3.48 (m, 2H), 3.60 (m, 2H), 3.76 (m, 2H), 4.20 (m, 2H), 7.11 (m, J_{AB} = 8.1Hz, 2H), 7.19 (m, J_{AB} = 9.0Hz, 2H), 7.49 (m, J_{AB} = 8.1Hz, 2H), 7.72 (m, J_{AB} = 9.0Hz, 2H), 7.90 (dd, *J* = 1.3, 1.9Hz, 1H), 8.23 (dd, *J* = 1.5, 1.9Hz, 1H), 9.61 (dd, *J* = 1.3, 1.5Hz, 1H). mp 113.0–116.0℃	72.1	32.4
化合物 88		(200 MHz, *DMSO-d_6*) δ 1.10 (t, *J* = 7.0Hz, 3H), 2.29 (s, 3H), 3.38–3.65 (m, 6H), 3.74–3.83 (m, 2H), 4.15–4.25 (m, 2H), 7.12 (m, J_{AB} = 7.9Hz, 2H), 7.20 (m, J_{AB} = 9.0Hz, 2H), 7.49 (m, J_{AB} = 8.1Hz, 2H), 7.72 (m, J_{AB} = 9.2Hz, 2H), 7.90 (dd, *J* = 1.3, 1.8Hz, 1H), 8.22 (dd, *J* = 1.5, 1.8Hz, 1H), 9.59 (dd, *J* = 1.3, 1.5Hz, 1H). mp 117.0–117.5℃	66.4	18.5
化合物 89		(200 MHz, *DMSO-d_6*) δ 0.88 (t, *J* = 7.0Hz, 3H), 1.23–1.60 (m, 4H), 2.29 (s, 3H), 3.46 (t, *J* = 8.4Hz, 2H), 3.69–3.75 (m, 2H), 4.13–4.23 (m, 2H), 7.11 (m, J_{AB} = 7.9Hz, 2H), 7.20 (m, J_{AB} = 9.0Hz, 2H), 7.48 (m, J_{AB} = 8.1Hz, 2H), 7.72 (m, J_{AB} = 9.0Hz, 2H), 7.90 (dd, *J* = 1.5, 1.8Hz, 1H), 8.22 (dd, *J* = 1.3, 1.8Hz, 1H), 9.59 (dd, *J* = 1.3, 1.5Hz, 1H). mp 137.0–139.0℃	96.7	4.1
化合物 90		*DMSO-d_6*, δ 2.17 (s, 1H), 2.29 (s, 3H), 2.88 (t, *J* = 6.6Hz, 1H), 4.24 (t, *J* = 6.6Hz, 2H), 7.12 (m, J_{AB} = 8.0Hz, 2H), 7.20 (m, J_{AB} = 9.2Hz, 2H), 7.49 (m, J_{AB} = 8.0Hz, 2H), 7.73 (m, J_{AB} = 9.2Hz, 2H), 7.90 (dd, *J* = 1.3, 1.9Hz, 1H), 8.23 (dd, *J* = 1.5, 1.9Hz, 1H), 9.61 (dd, *J* = 1.3, 1.5Hz, 1H). mp 140.0–142.0℃	91.8	7.5

[0061]
[Table 14]

化合物 97		(200 MHz, *DMSO-d_6*) δ 2.29 (s, 3H), 2.45-2.58 (m, 2H), 4.12 (t, *J* = 6.6Hz, 2H), 5.05-5.25 (m, 2H), 5.90 (m, 1H), 7.11 (m, J_{AB} = 7.9Hz, 2H), 7.19 (m, J_{AB} = 9.0Hz, 2H), 7.48 (m, J_{AB} = 8.1Hz, 2H), 7.71 (m, J_{AB} = 9.0Hz, 2H), 7.90 (dd, *J* = 1.5, 1.8Hz, 1H), 8.21 (dd, *J* = 1.3, 1.8Hz, 1H), 9.58 (dd, *J* = 1.3, 1.5Hz, 1H). mp 133.5-134.5℃	101.9	2.5
化合物 98		(200 MHz, *DMSO-d_6*) δ 1.13-2.05 (m, 10H), 2.29 (s, 3H), 4.47(m, 1H), 7.11 (m, J_{AB} = 7.7Hz, 2H), 7.18 (m, J_{AB} = 9.0Hz, 2H), 7.48 (m, J_{AB} = 8.1Hz, 2H), 7.68 (m, J_{AB} = 9.0Hz, 2H), 7.89 (dd, *J* = 1.5, 1.8Hz, 1H), 8.20 (dd, *J* = 1.3, 1.8Hz, 1H), 9.56 (dd, *J* = 1.3, 1.5Hz, 1H). mp 187.5-188.0℃	96.2	3.7
化合物 99		*DMSO-d_6*, δ 0.99 (d, *J* = 6.6Hz, 6H), 2.05 (m, 1H), 2.29 (s, 3H), 3.84 (d, *J* = 6.6Hz, 2H), 7.11 (d, J_{AB}= 8.1Hz, 2H), 7.18 (m, J_{AB} = 9.0Hz, 2H), 7.48 (m, J_{AB} = 8.1Hz, 2H), 7.71 (m, J_{AB}= 9.0Hz, 2H), 7.88 (t, *J* = 1.5, 1.8Hz, 1H), 8.20 (t, *J* = 1.3, 1.8Hz, 1H), 9.55 (t, *J* = 1.3, 1.5Hz, 1H). mp 176.5-178.0℃	100.6	4.3
化合物 100		(200 MHz, *DMSO-d_6*) δ 2.05-2.23 (m, 2H), 2.99 (t, *J* =7.9Hz, 2H), 4.11 (t, *J* = 6.4Hz, 2H), 7.16 (m, J_{AB} = 9.2Hz, 2H), 7.74 (m, J_{AB} = 9.2Hz, 2H), 7.88-8.03 (m, 2H), 8.23 (dd, *J* = 1.3, 1.8Hz, 1H), 8.48 (m, 1H), 8.77 (dd, *J* = 0.9 5.5Hz, 1H), 8.86 (d, *J* = 2.0Hz, 1H), 9.69 (dd, *J* = 1.3, 1.5Hz, 1H). mp 252.0-253.0℃	99.1	1.1
化合物 101		(200 MHz, *DMSO-d_6*) δ 1.28-1.85 (m, 8H), 2.69 (s, 3H), 2.72 (s, 3H), 2.91-3.10 (m, 2H), 4.07 (t, *J* = 6.4Hz, 2H), 7.18 (m, J_{AB} = 9.2Hz, 2H), 7.73 (m, J_{AB} = 9.0Hz, 2H), 7.89 (dd, *J* = 1.5, 1.8Hz, 1H), 8.22 (dd, *J* = 1.3, 1.8Hz, 1H), 9.65 (dd, *J* = 1.3, 1.5Hz, 1H). mp 205.0-207.0℃	90.0	2.2
化合物 102		δ 0.96 (t, *J* = 7.3 Hz, 3H), 1.35-1.42 (m, 2H), 1.58-1.68 (m, 2H), 2.18 (s, 3H), 2.67 (t, *J* = 7.6 Hz, 2H), 7.21-7.28 (m, 4H), 7.62 (dd, *J* = 1.4, 1.7Hz, 1H), 8.74 (dd, *J* = 1.2, 1.4Hz, 1H). mp 152.0-153.0℃		

[0063]
[Table 16]

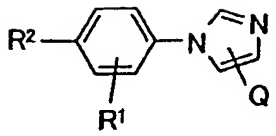
[0065]
[Table 18]

化合物 110	 TsOH	*DMSO-d_6*, δ 1.21 (t, *J* = 7.5Hz, 3H), 2.29 (s, 3H), 2.64 (q, *J* = 7.5Hz, 2H), 2.91 (t, *J* = 6.6Hz, 2H), 4.23 (t, *J* = 6.6Hz, 2H), 7.11 (d, *J* = 7.9Hz, 2H), 7.20 (m, J_{AB} = 9.2Hz, 2H), 7.49 (d, *J* = 7.9Hz, 2H), 7.73 (m, J_{AB} = 9.2Hz, 2H), 7.90 (dd, *J* = 1.3, 1.9Hz, 1H), 8.22 (dd, *J* = 1.5, 1.9Hz, 1H), 9.61 (dd, *J* = 1.3, 1.5Hz, 1H). mp 147.0-149.0°C	97.9	1.8
化合物 111	 CH CH	*DMSO-d_6*, δ 1.28 (t, *J* = 7.3Hz, 6H), 3.10-3.30 (m, 4H), 3.46-3.58 (m, 2H), 4.51 (t, *J* = 5.0Hz, 2H), 7.25 (m, J_{AB} = 9.0Hz, 2H), 7.78 (m, J_{AB} = 8.9Hz, 2H), 7.90 (dd, *J* = 1.5, 1.8Hz, 1H), 8.23 (dd, *J* = 1.3, 1.8Hz, 1H), 9.66 (dd, *J* = 1.3, 1.5Hz, 1H). mp 228.0-230.0°C	33.0	49.5
化合物 112	 2 HCl	*DMSO-d_6*, δ 2.73 (s, 3H), 5.52 (s, 2H), 7.32 (m, J_{AB} = 9.2Hz, 2H), 7.68 (d, *J* = 7.9Hz, 1H), 7.73-7.83 (m, 3H), 7.92 (dd, *J* = 1.5, 1.8Hz, 1H), 8.20-8.30 (m, 2H), 9.72 (dd, *J* = 1.3, 1.5Hz, 1H). mp 236.0-237.0°C	80.4	17.6
化合物 113	 2 HCl	*DMSO-d_6*, δ 1.26 (m, 1H), 1.88 (m, 2H), 2.73 (s, 1H), 2.73-2.87 (m, 2H), 3.26-3.51 (m, 2H), 3.93 (dd, *J* = 7.3, 9.6Hz, 1H), 4.05 (dd, *J* = 4.7, 9.6Hz, 1H), 7.19 (m, J_{AB} = 9.0Hz, 2H), 7.75 (m, J_{AB} = 9.0Hz, 2H), 7.90 (d, *J* = 1.4Hz, 1H), 8.23 (d, *J* = 1.4Hz, 1H), 9.65 (d, *J* = 1.4Hz, 1H). mp 232.0-242.0°C	82.2	6.8
化合物 114		δ 3.09 (t, *J* = 4.5Hz, 4H), 3.90 (t, *J* = 4.5Hz, 4H), 7.12 (d, *J* = 8.7Hz, 1H), 7.20 (s, 1H), 7.22 (s, 1H), 7.27 (dd, *J* = 2.5, 8.7Hz, 1H), 7.45 (d, *J* = 2.5Hz, 1H), 7.79 (s, 1H). mp 127.0-129.0°C		40.8
化合物 115	 2 TsOH	*DMSO-d_6*, δ 2.29 (s, 6H), 2.89 brs, 6H), 3.57 (m, 2H), 4.41 (brt, *J* = 5.3Hz, 2H), 7.12 (brd, *J* = 7.9Hz, 4H), 7.25 (m, J_{AB} = 9.0Hz, 2H), 7.49 (brd, *J* = 7.9Hz, 4H), 7.77 (m, J_{AB} = 9.0Hz, 2H), 7.93 (t, *J* = 1.5Hz, 1H), 8.24 (t, *J* = 1.5Hz, 1H), 9.63 (d, *J* = 1.5Hz, 1H). mp 161.0-164.0°C	19.4	387.4
化合物 116	 2 HCl	*DMSO-d_6*, δ 2.76 (s, 3H), 2.77 (s, 3H), 3.27 (m, 2H), 3.80-3.91 (m, 4H), 4.25 (m, 2H), 7.21 (m, J_{AB} = 9.0Hz, 2H), 7.76 (m, J_{AB} = 9.0Hz, 2H), 7.91 (dd, *J* = 1.3, 1.9Hz, 1H), 8.24 (dd, *J* = 1.5, 1.9Hz, 1H), 9.71 (dd, *J* = 1.3, 1.5Hz, 1H). mp 174.0-179.0°C	57.2	9.0

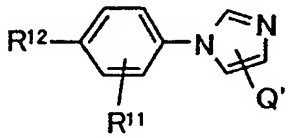
20-HETE production inhibitory action was examined about the compound given [above-mentioned] in a table.
The exam was performed based on J.Pharmacol.Exp.Ther., the 268th volume, and the approach of a page [474th] (1994) publication.
3-morpholino propane sulfonic acid of 50mM(s) which contain the magnesium chloride of 5mM, and ethylenediamine tetra-acetic acid JISODIUMUSORUTO (EDTA) of 1mM for the test drug solution prepared to 1microM by DMSO (MOPS) (pH7.4) It adds to the buffer solution. As a source of an enzyme, a Homo sapiens kidney microsome fraction (Human Cell Culture Center, Anatomic Gift Foundation), The [5, 6, 8, 9, 11, 12, 14, 15] tritium-arachidonic acid was added as a substrate, NADPH was added as a coenzyme, and it was made to react at 37 degrees for 1.5 hours. After adding the formic acid to reaction mixture and making it suspend a reaction, the acetonitrile (50% of final concentration) was added. The amount of production of 20-HETE was measured using the high performance chromatography with a radioactive substance detector equipped with an ODS column (the biotechnology sill C18, Bio-Rad make).
[0067]
The amount of production of 20-HETE at the time of compound additive-free was made into 100%, and the rate of control (%) was computed from the amount of 20-HETE production when adding a compound. The result is collectively shown in the above-mentioned table 1.
Moreover, the amount of production of 20-HETE at the time of compound additive-free was made into 100%, and the 20-HETE production when adding a compound also computed the compound concentration (IC50 value) checked 50%. The result is also collectively shown in the above-mentioned table 1.

[Translation done.]

【特許請求の範囲】
【請求項１】
式
【化１】



｛式中、Ｑは水素原子またはＣ１～Ｃ４アルキル基であり、Ｒ１は、水素原子、Ｃ１～Ｃ６アルキル基、ハロゲン原子であり、Ｒ２はＣ１～Ｃ１４アルキル基、Ｃ２～Ｃ１４アルカノイル基、モルホリノ基又は式Ｒ３－Ｏ－［式中、Ｒ３はＣ１～Ｃ１４アルキル基、Ｃ２～Ｃ１４アルケニル基、Ｃ３～Ｃ１４アルキニル基、Ｃ３～Ｃ１０シクロアルキル基、１－フェニル－２－プロピニル基又は式Ｒ４－Ａ－（式中、Ｒ４はＣ３～Ｃ１０シクロアルキル基、Ｃ１～Ｃ１０アルコキシ基、Ｃ２～Ｃ１０アルカノイル基、Ｃ２～Ｃ６アルコキシカルボニル基、ジオキソラニル基、Ｃ１～Ｃ６アルキル基で置換されたジオキソラニル基、オキサニル基、ジオキサニル基、Ｃ１～Ｃ６アルキル基で置換されたジオキサニル基、ベンゾジオキサニル基、ビシクロ［２．２．１］ヘプタン－２－イル基、Ｃ１～Ｃ６アルキルチオ基、ピロリジニル基、Ｃ１～Ｃ６アルキル基で置換されたピロリジニル基、ピペリジニル基、Ｃ１～Ｃ６アルキル基で置換されたピペリジニル基、モルホリノ基、４－Ｃ２～Ｃ６アルコキシカルボニルピペラジン－１－イル基、ピロリル基、ピリジル基、Ｎ，Ｎ－ジＣ１～Ｃ６アルキルアミノ基、Ｎ，Ｎ－ジＣ１～Ｃ６アルキルアミノＣ１～Ｃ６アルコキシ基、Ｃ１～Ｃ６アルコキシＣ１～Ｃ６アルコキシ基、フェノキシ基、フェニル基、「Ｃ１～Ｃ６アルキル基、Ｃ１～Ｃ６アルコキシ基、ハロゲン原子、フェニルエチル基、フェノキシ基、ニトリル及びメチルチオ基」から選ばれる基の１又は２個で置換されたフェニル基、ビフェニル基、フェニルチオ基、フリル基、チエニル基、チアゾリル基、Ｃ１～Ｃ６アルキル基で置換されたチアゾリル基、トルイジノ基、Ｎ－Ｃ１～Ｃ６アルキルトルイジノ基、ピロリドン－１－イル基であり、ＡはＣ１～Ｃ１０アルキレン基である。）で示される基である。］で示される基である。｝で表されるイミダゾール誘導体又はその製薬学的に許容される塩を有効成分として含むことを特徴とする２０－ＨＥＴＥ産生酵素阻害剤。
【請求項２】
式
【化２】



｛式中、Ｑ’は水素原子またはＣ１～Ｃ４アルキル基であり、Ｒ１１は、水素原子、Ｃ１～Ｃ６アルキル基、ハロゲン原子であり、Ｒ１２はモルホリノ基又は式Ｒ１３－Ｏ－［式中、Ｒ１３は、Ｃ３～Ｃ１４アルキニル基、Ｃ３～Ｃ１０シクロアルキル基、１－フェニル－２－プロピニル基又は式Ｒ１４－Ａ’－（式中、Ｒ１４はＣ３～Ｃ１０シクロアルキル基、Ｃ１～Ｃ１０アルコキシ基、Ｃ２～Ｃ１０アルカノイル基、ジオキソラニル基、Ｃ１～Ｃ６アルキル基で置換されたジオキソラニル基、オキサニル基、ジオキサニル基、Ｃ１～Ｃ６アルキル基で置換されたジオキサニル基、ベンゾジオキサニル基、ビシクロ［２．２．１］ヘプタン－２－イル基、Ｃ１～Ｃ６アルキルチオ基、４－Ｃ２～Ｃ６アルコキシカルボニルピペラジン－１－イル基、ピロリル基、Ｎ，Ｎ－ジＣ１～Ｃ６アルキルアミノＣ１～Ｃ６アルコキシ基、Ｃ１～Ｃ６アルコキシＣ１～Ｃ６アルコキシ基、フリル基、チエニル基、ピロリドン－１－イル基であり、Ａ’はＣ１～Ｃ１０アルキレン基である。

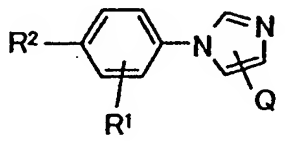
する芳香族化合物、特に様々な置換基を有する１－（４－置換フェニル）－１Ｈ－イミダゾール誘導体が意外にも選択的に２０－ＨＥＴＥの産生酵素の阻害作用を有することを見出し、本発明を完成した。

【０００７】

すなわち、本発明は、下記式（１）

【０００８】

【化３】



(1)

【０００９】

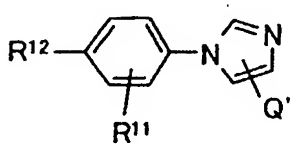
｛式中、Ｑは水素原子またはC_1～C_4アルキル基であり、R^1は、水素原子、C_1～C_6アルキル基、ハロゲン原子であり、R^2はC_1～C_{14}アルキル基、C_2～C_{14}アルカノイル基、モルホリノ基又は式R^3－Ｏ－［式中、R^3は、C_1～C_{14}アルキル基、C_2～C_{14}アルケニル基、C_3～C_{14}アルキニル基、C_3～C_{10}シクロアルキル基、１－フェニル－２－プロピニル基又は式R^4－Ａ－（式中、R^4はC_3～C_{10}シクロアルキル基、C_1～C_{10}アルコキシ基、C_2～C_{10}アルカノイル基、C_2～C_6アルコキシカルボニル基、ジオキソラニル基、C_1～C_6アルキル基で置換されたジオキソラニル基、オキサニル基、ジオキサニル基、C_1～C_6アルキル基で置換されたジオキサニル基、ベンゾジオキサニル基、ビシクロ［２．２．１］ヘプタン－２－イル基、C_1～C_6アルキルチオ基、ピロリジニル基、C_1～C_6アルキル基で置換されたピロリジニル基、ピペリジニル基、C_1～C_6アルキル基で置換されたピペリジニル基、モルホリノ基、４－C_2～C_6アルコキシカルボニルピペラジン－１－イル基、ピロリル基、ピリジル基、Ｎ，Ｎ－ジC_1～C_6アルキルアミノ基、Ｎ，Ｎ－ジC_1～C_6アルキルアミノC_1～C_6アルコキシ基、C_1～C_6アルコキシC_1～C_6アルコキシ基、フェノキシ基、フェニル基、「C_1～C_6アルキル基、C_1～C_6アルコキシ基、ハロゲン原子、フェニルエチル基、フェノキシ基、ニトリル及びメチルチオ基」から選ばれる基の１又は２個で置換されたフェニル基、ビフェニル基、フェニルチオ基、フリル基、チエニル基、チアゾリル基、C_1～C_6アルキル基で置換されたチアゾリル基、トルイジノ基、Ｎ－C_1～C_6アルキルトルイジノ基、ピロリドン－１－イル基であり、ＡはC_1～C_{10}アルキレン基である。）で示される基である。］で示される基である。｝で表されるイミダゾール誘導体又はその製薬学的に許容される塩を有効成分として含むことを特徴とする２０－ＨＥＴＥ産生酵素阻害剤である。

【００１０】

また、他の本発明は下記式（２）

【００１１】

【化４】

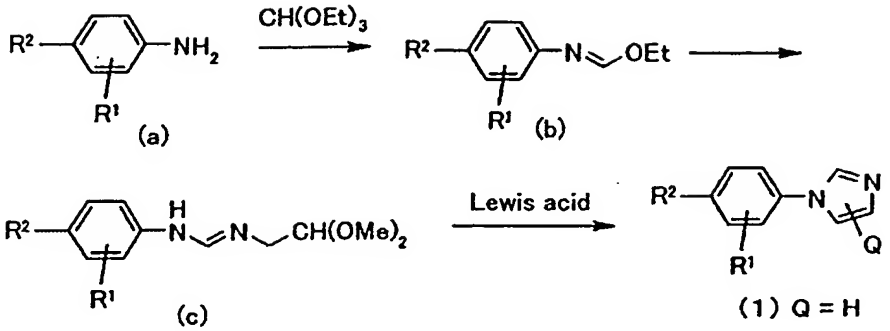


(2)

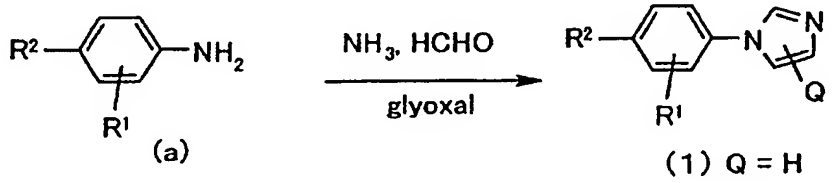
【００１２】

｛式中、Ｑ’は水素原子またはC_1～C_4アルキル基であり、R^{11}は、水素原子、C_1

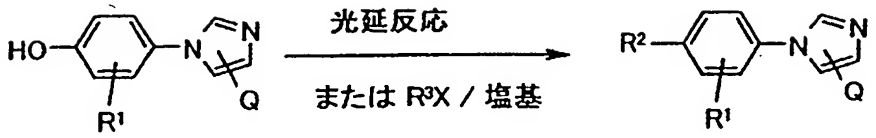
【００１８】
C_1～C_6アルコキシC_1～C_6アルコキシ基は、C_1～C_6アルコキシ基とC_1～C_6アルコキシ基が複合した形態を有するものであり、C_1～C_4アルコキシC_1～C_4アルコキシ基が好ましい。中でも、メトキシエトキシ基、ｎ－ブトキシエトキシ基などがより好ましい。
C_2～C_6アルコキシカルボニル基は、炭素原子を２～５個有する直鎖状又は分枝状のアルコキシ基と１個のカルボニル基（－ＣＯ－）が複合した形態を有するものであり、C_2～C_4アルコキシカルボニル基が好ましい。中でも、メトキシカルボニル基、エトキシカルボニル基などがより好ましい。
【００１９】
ジオキソラニル基は、ヘテロ原子として酸素原子を２個有する飽和五員環（ジオキソラン）、好ましくは１，３－ジオキソランの環から水素を除いて誘導される１価の基を意味する。
オキサニル基は、ヘテロ原子として酸素原子を１個有する飽和六員環の形態を有するもので、２－オキサニル基、３－オキサニル基を含む。
ジオキサニル基は、ヘテロ原子として酸素原子を２個有する飽和六員環（ジオキサン）、好ましくは１，３－ジオキサンの環から水素を除いて誘導される１価の基を意味する。C_1～C_6アルキル基で置換されたジオキサニル基は、その基の環がC_1～C_6アルキル基で置換されていてもよく、例えば５，５－ジメチル－１，３－ジオキサン－２－イル基などである。
【００２０】
C_1～C_6アルキルチオ基は、炭素原子を１～６個有する直鎖状又は分枝状のアルキル基と１個のチオ基（－Ｓ－）が複合した形態を有しており、C_1～C_4アルキルチオ基が好ましい。例えば、メチルチオ基、エチルチオ基などがより好ましい。
【００２１】
ピロリジニル基は、ピロリジンの環状の窒素原子又は炭素原子上から水素原子を除いて誘導される１価の基を意味し、例えば、１－ピロリジニル基、２－ピロリジニル基、３－ピロリジニル基などが挙げられる。C_1～C_6アルキル基で置換されたピロリジニル基は、その基上の少なくとも１つの水素原子がC_1～C_6アルキル基、好ましくはC_1～C_4アルキル基によって置換されたピロリジニル基であり、例えば、Ｎ－メチルピロリジン－２－イル基などが挙げられる。
ピペリジニル基は、ピペリジンの炭素原子上から水素原子を除いて誘導される１価の基を意味する。C_1～C_6アルキル基で置換されたピペリジニル基は、その基の窒素原子がC_1～C_6アルキル基によって置換されたピペリジニル基であり、例えば、Ｎ－メチルピペリジン－２－イル基、Ｎ－メチルピペリジン－３－イル基などが挙げられる。
４－C_2～C_6アルコキシカルボニルピペラジン－１－イル基は、ピペラジンの４位の窒素原子がC_2～C_6アルコキシカルボニル基で修飾され、１位の窒素原子上から水素原子を除いて誘導される１価の基を意味する。
モルホリノ基は、モルホリンの窒素原子上から水素原子を除いて誘導される１価の基を意味する。
【００２２】
フリル基は、２－フリル基、３－フリル基を含む。
チエニル基は、２－チエニルル基、３－チエニル基を含む。
チアゾリル基は、２－チアゾリル基、４－チアゾリル基、５－チアゾリル基を含む。また、C_1～C_6アルキル基で置換されたチアゾリル基は、その環上の少なくとも１つの水素原子がC_1～C_6アルキル、好ましくはC_1～C_4アルキル基、より好ましくはメチル基によって置換されたチアゾリル基であり、例えば４－メチルチアゾール－５－イル基などが挙げられる。
ピリジル基は、２－ピリジル基、３－ピリジル基、４－ピリジル基を含む。　ピロリル基は、１－ピロリル基、２－ピロリル基、３－ピロリル基を含み、１－ピロリル基（Ｎ－ピ



【００２９】
製造法１；Ｊ．Ｈｅｔｅｒｏｃｙｃｌｉｃ Ｃｈｅｍ．，第２５巻，１６４９項（１９８８）を参照にアニリン誘導体（ａ）を酢酸または塩酸等の酸触媒の存在下或いは非存在下に、オルトギ酸トリメチル、オルトギ酸トリエチル等のオルトギ酸エステル類と、反応させ、イミノエーテル誘導体（ｂ）を得る。反応温度は室温から１５０℃、好ましくは７０～１００℃で反応時間は２～７２時間である。次に、イミノエーテル誘導体（ｂ）を適当な溶媒中（メタノール、エタノール、プロパノール、テトラヒドロフラン、ジオキサン、トルエン、塩化メチレン、クロロホルム、アセトニトリル、酢酸エチル、ジメチルスルホキシド、ジメチルホルムアミド等）アミノアセトアルデヒドジメチルアセタールと反応させホルムアミジン誘導体（ｃ）を得る。この時の反応温度は室温～１５０℃、好ましくは７０～１００℃であり、反応時間は２～２４時間である。次に、ホルムアミジン誘導体（ｃ）を適当な溶媒中（エーテル、テトラヒドロフラン、ジメトキシエタン、ジオキサン等）にルイス酸あるいは酸触媒（四塩化チタン、トリフルオロボランエーテラート、酢酸等）の共存下反応させ、本発明化合物（１）を合成することができる（式中Ｒ^{1}、Ｒ^{2}は前記と同義である）。また、この方法で合成した本発明化合物（１）のＲ^{2}を相互に変換することによって他の本発明化合物（１）に導くこともできる。
【００３０】
【化６】



【００３１】
製造法２；化合物（１）はアニリン誘導体（ａ）から直接合成することもできる。すなわち、アニリン誘導体とアンモニア、ホルムアルデヒド、そしてグリオキサールを１：１：１：１の比率で混合し水またはアルコール／水の混合溶媒中にて、反応温度は室温～１５０℃、好ましくは７０～１２０℃で反応することによって本発明化合物（１）を合成することができる（式中Ｒ^{1}、Ｒ^{2}は前記と同義である）。
【００３２】
【化７】



(g) (1)

【００３７】
次に、４－（イミダゾール－１－イル）－フェノール誘導体（ｈ）と対応する種々のアルコールを光延反応（Ｏｒｇ．　Ｒｅａｃｔｉｏｎｓ，第４２巻，第３３５項）を利用し製造することができる。すなわち、化合物（ｈ）を適当な溶媒（テトラヒドロフラン、ジオキサン、トルエン、塩化メチレン、クロロホルム、アセトニトリル、酢酸エチル、ジメチルスルホキシド、ジメチルホルムアミド等）中で、ホスフィン試薬（トリフェニルホスフィン、トリブチルホスフィンやジフェニル－２－ピリジルホスフィン等）、ジアゾ試薬（ジエチルアゾジカルボキシレートやジ－ｔｅｒｔ－ブチルアゾジカルボキシレート等）、及び対応する種々のアルコール類とを、０℃～室温、好ましくは室温にて２～１２時間反応し、本発明化合物（１）（式中記号は前記と同意義である。）を製造することができる。或いは、種々のハロゲン化アルキル類（R^3X、Ｘはハロゲンを表し、その他の記号は前記と同義である）と、適当な溶媒（アセトン、ジメチルホルムアミド、テトラヒドロフラン、エーテル等）中適当な塩基（トリエチルアミン、Ｎ，Ｎ－ジイソプロピルエチルアミン、ピリジン、炭酸カリウム、炭酸カルシウム、炭酸セシウム、水素化ナトリウム、ナトリウムメトキシド、ｔ－ブトキシカリウム等）の存在下、で、０℃～室温、好ましくは室温にて２～２４時間反応し、R^2がR^3Oである本発明化合物（１）を製造することができる。

【００３８】
本発明化合物及びその製薬学的に許容される塩は、経口又は非経口的に投与することができる。その投与剤型は錠剤、カプセル剤、顆粒剤、散剤、粉剤、トローチ剤、軟膏剤、クリーム剤、乳剤、懸濁剤、坐剤、注射剤などであり、いずれも慣用の製剤技術（例えば、第１４改正日本薬局方に規定する方法）によって製造することができる。これらの投与剤型は、患者の症状、年齢及び治療の目的に応じて適宜選択することができる。各種剤型の製剤の製造においては、常用の賦形剤（例えば、結晶セルロース、デンプン、乳糖、マンニトールなど）、結合剤（例えば、ヒドロキシプロピルセルロース、ポリビニルピロリドンなど）、滑沢剤（例えば、ステアリン酸マグネシウム、タルクなど）、崩壊剤（例えば、カルボキシメチルセルロースカルシウムなど）などを用いることができる。

【００３９】
本発明に係る化合物並びにその製薬学的に許容される塩の投与量は、成人を治療する場合で１日１～２０００ｍｇであり、これを１日１回又は数回に分けて投与する。この投与量は、患者の年齢、体重及び症状によって適宜増減することができる。

【００４０】
【発明の効果】
本発明に係る化合物及びその製薬学的に許容される塩は、優れた２０－ＨＥＴＥ産生阻害作用を有し、溶解度などの物性的にも優れるものである。従って、本発明に係る化合物は、ヒト及び動物における２０－ＨＥＴＥが関わる疾病、例えば各種腎疾患、脳血管疾患、各種循環器疾患治療薬として有用である。

【００４１】
【実施例】
以下、実施例を挙げて本発明を更に詳しく説明する。
実施例１
１－［４－プロピルフェニル］－イミダゾール塩酸（化合物１０８）の製造
４－プロピルアニリン　（２．０３ｇ，　０．０１５０ｍｏｌ）とオルトギ酸トリエチル

有機層を飽和食塩水洗浄後、硫酸マグネシウムで乾燥し、濃縮した。得られた残査をＮＨ型シリカゲルクロマトグラフィー（ヘキサン－酢酸エチル＝１：２）で精製し１－［４－プロピルオキシフェニル］－１Ｈ－イミダゾール　（１．１７ｇ，　９２％）を無色油状物として得た。これをエタノールに溶解しｐ－トルエンスルホン酸１水和物　（１．１ｇ，　５．７８ｍｍｏｌ）のエタノール溶液を加え析出した結晶を濾過し、無色粉末状の標題化合物　（１．９８ｇ，　８５％）を得た。融点１４８．０－１５０．０℃

【００４４】

実施例４

１－［４－ブトキシフェニル］－２－メチル－イミダゾールトルエンスルホネート（化合物１１７）の製造

（１）４－メトキシフェニルボレート　（３．７ｇ，　２４．４ｍｍｏｌ）と１－Ｈ－２－メチルイミダゾール　（１．０ｇ，　１２．２ｍｍｏｌ）、塩化メチレン　（４８ｍＬ）の混合物に、［Ｃｕ（ＯＨ）ＴＭＥＤＡ］$_2$Ｃｌ$_2$（０．５７ｇ，　１．２２ｍｍｏｌ）を加え、酸素雰囲気下、室温にて１８時間撹拌した。反応混合物を濾過して不溶物を除いた後、濾液を濃縮した。得られた残査をＮＨ型シリカゲルクロマトグラフィー（ヘキサン－酢酸エチル＝４：１）で精製し、１－［４－メトキシフェニル］－２－メチル－イミダゾール　（２．３５ｇ）を得た。

【００４５】

（２）１－［４－メトキシフェニル］－２－メチル－イミダゾール　（２．０ｇ）と４８％臭化水素　（２０ｍＬ）の混合物を１００℃で１６時間反応した。反応液を室温に冷却した後に、６Ｍ水酸化ナトリウムで中和後析出した結晶を濾過し、４－（２－メチル－イミダゾール－１－イル）フェノール　（０．７５ｇ，　４０％）を得た。

【００４６】

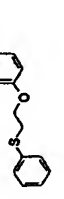
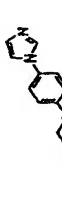
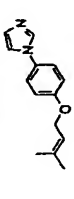
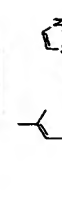
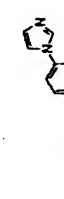
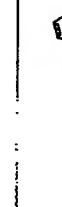
（３）４－（２－メチル－イミダゾール－１－イル）フェノール　（０．２０ｇ，　１．２ｍｍｏｌ）とジメチルホルムアミド　（２ｍＬ）溶液に、１－イオド－ｎ－ブタン　（０．２５ｇ，　１．３８ｍｍｏｌ）と炭酸カリウム　（０．１９ｇ，　１．３８ｍｍｏｌ）を加え、室温で６４時間撹拌した。反応液に水を加え、ヘキサン－酢酸エチル＝１：１の混合溶媒で抽出した。有機層を飽和食塩水で洗浄後、硫酸マグネシウムで乾燥し、濃縮した。得られた残査をＮＨ型シリカゲルクロマトグラフィー（ヘキサン－酢酸エチル＝４：１）で精製し、１－［４－ブトキシフェニル］－２－メチル－イミダゾール　（０．１７ｇ，　６４％）を得た。これをエタノールに溶解しｐ－トルエンスルホン酸１水和物のエタノール溶液を加え、析出した結晶を濾過し、無色粉末状の標題化合物　（０．１８ｇ，　３９％）を得た。融点１４８．０－１４９．０℃

【００４７】

各々対応する出発原料を用いて実施例１～４と同様な反応操作を行うことにより、表１に示す化合物を合成した。尚、表１には実施例１～４で合成した化合物を併せて標記した。

【００４８】

【表１】

化合物 8		δ 2.34 (s, 3H), 3.09 (t, J = 7.1Hz, 2H), 4.18 (t, J = 7.1Hz, 2H), 6.97 (m, J_{AB} = 9.0Hz, 2H), 7.13-7.20 (m, 4H), 7.27 (m, J_{AB} = 9.0Hz, 2H), 7.75 (s, 1H).	105.9
化合物 9		δ 3.32 (t, J = 6.9Hz, 2H), 4.18 (t, J = 6.9Hz, 2H), 6.93 (m, J_{AB} = 9.0Hz, 2H), 7.18 (s, 1H), 7.19 (s, 1H), 7.21-7.35 (m, 5H), 7.43 (m, J_{AB} = 9.0Hz, 2H), 7.75 (s, 1H).	99.0
化合物 10		δ 2.56 (t, J = 2.5Hz, 1H), 4.75 (d, J = 2.5Hz, 2H), 7.08 (m, J_{AB} = 9.0Hz, 2H), 7.10 (s, 1H), 7.19 (s, 1H), 7.33 (m, J_{AB} = 9.0Hz, 2H), 7.77 (s, 1H).	42.9
化合物 11		δ 1.77 (s, 3H), 1.82 (s, 3H), 4.55 (d, J = 6.7Hz, 2H), 5.50 (m, 1H), 6.99 (m, J_{AB} = 8.9Hz, 2H), 7.18 (s, 1H), 7.21 (s, 1H), 7.29 (m, J_{AB} = 8.9Hz, 2H), 7.76 (s, 1H).	93.8
化合物 12		δ 1.62 (s, 3H), 1.69 (s, 3H), 1.82 (s, 3H), 2.15 (m, 4H), 4.54 (d, J = 6.8Hz, 2H), 5.12 (m, 1H), 5.51 (t, J = 6.8Hz, 1H), 6.99 (m, J_{AB} = 8.9Hz, 2H), 7.19 (s, 1H), 7.21 (s, 1H), 7.29 (m, J_{AB} = 8.9Hz, 2H), 7.76 (s, 1H).	91.9
化合物 13		δ 1.78 (dd, J = 1.4, 6.2Hz, 3H), 4.50 (dt, J = 1.2, 5.9Hz, 2H), 5.69-5.96 (m, 2H), 6.98 (m, J_{AB} = 9.0Hz, 2H), 7.18 (s, 1H), 7.20 (s, 1H), 7.28 (m, J_{AB} = 8.9Hz, 2H), 7.76 (s, 1H).	104.9
化合物 14		δ 1.78 (d, J = 6.8Hz, 3H), 4.58 (d, J = 6.2Hz, 2H), 5.73-5.81 (m, 2H), 6.10 (m, 1H), 6.35 (dd, J = 10.7, 15.7Hz, 3H), 6.99 (m, J_{AB} = 8.9Hz, 2H), 7.18 (s, 1H), 7.20 (s, 1H), 7.29 (m, J_{AB} = 8.9Hz, 2H), 7.76 (s, 1H).	98.1

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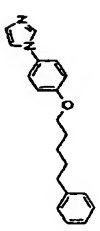
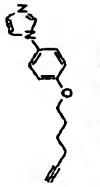
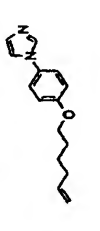
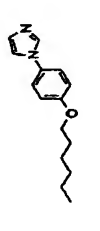
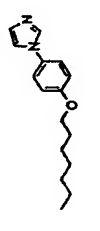
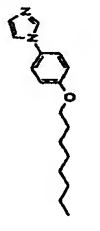
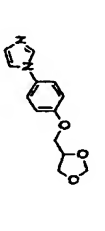
【表３】

化合物 22		δ 1.47–1.89 (m, 6H), 2.66 (t, J = 7.5Hz, 2H), 3.98 (t, J = 6.5Hz, 2H), 6.96 (m, J_{AB} = 8.9Hz, 2H), 7.18–7.20 (m, 5H), 7.26–7.31 (m, 4H), 7.76 (s, 1H).	88.5
化合物 23		δ 1.74 (m, 2H), 1.92 (m, 2H), 1.98 (t, J = 2.6Hz, 2H), 2.30 (dt, J = 2.6, 7.0Hz, 2H), 4.03 (t, J = 6.3Hz, 2H), 6.96 (m, J_{AB} = 8.9Hz, 2H), 7.18 (s, 1H), 7.20 (s, 1H), 7.29 (m, J_{AB} = 8.9Hz, 2H), 7.76 (s, 1H).	99.5
化合物 24		δ 1.60 (m, 2H), 1.83 (quint, J = 7.0Hz, 2H), 2.14 (q, J = 7.0Hz, 2H), 4.00 (t, J = 6.5Hz, 2H), 4.98–5.08 (m, 2H), 5.77–5.91 (m, 1H), 8.97 (m, J_{AB} = 8.9Hz, 2H), 7.18 (s, 1H), 7.20 (s, 1H), 7.29 (m, J_{AB} = 8.9Hz, 2H), 7.76 (s, 1H).	99.1
化合物 25		δ 0.92 (t, J = 7.0Hz, 3H), 1.33–1.39 (m, 4H), 1.47 (m, 2H), 1.81 (m, 2H), 3.99 (t, J = 6.7Hz, 2H), 6.97 (m, J_{AB} = 8.9Hz, 2H), 7.18 (s, 1H), 7.20 (s, 1H), 7.29 (m, J_{AB} = 8.9Hz, 2H), 7.76 (s, 1H).	96.6
化合物 26		δ 0.90 (t, J = 6.8Hz, 3H), 1.25–1.45 (m, 8H), 1.81 (quint, J = 6.8Hz, 2H), 3.99 (t, J = 6.8Hz, 2H), 6.98 (m, J_{AB} = 8.9Hz, 2H), 7.18 (s, 1H), 7.20 (s, 1H), 7.29 (m, J_{AB} = 8.9Hz, 2H), 7.76 (s, 1H).	91.5
化合物 27		δ 0.89 (t, J = 6.8Hz, 3H), 1.23–1.54 (m, 10H), 1.79 (quint, J = 6.8Hz, 2H), 3.99 (t, J = 6.8Hz, 2H), 6.97 (m, J_{AB} = 9.0Hz, 2H), 7.18 (s, 1H), 7.20 (s, 1H), 7.29 (m, J_{AB} = 9.0Hz, 2H), 7.76 (s, 1H).	66.0
化合物 28		δ 3.89 (m, 1H), 3.99–4.18 (m, 3H), 4.46 (dt, J = 5.5, 7.7Hz, 2H), 4.95 (s, 1H), 5.11 (s, 1H), 7.01 (m, J_{AB} = 9.0Hz, 2H), 7.19 (s, 1H), 7.20 (s, 1H), 7.31 (m, J_{AB} = 9.0Hz, 2H), 7.77 (s, 1H).	80.3

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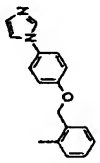
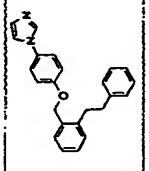
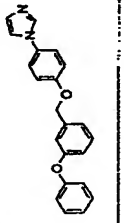
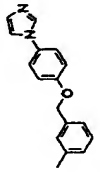
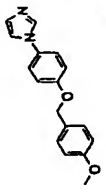
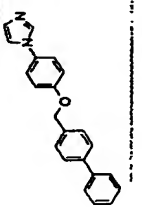
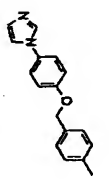
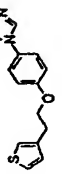
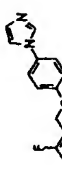
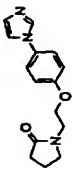
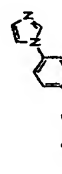
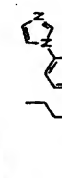
【表５】

化合物 36		δ 2.40 (s, 3H), 5.08 (s, 2H), 7.07 (m, J_{AB} = 8.9Hz, 2H), 7.19 (s, 1H), 7.21 (s, 1H), 7.23-7.33 (m, 5H), 7.41 (d, J = 7.3Hz, 1H), 7.77 (s, 1H).	100.5
化合物 37		δ 2.92-3.03 (m, 4H), 4.98 (s, 2H), 7.02 (m, J_{AB} = 8.9Hz, 2H), 7.12-7.36 (m, 10H), 7.41 (d, J = 7.8Hz, 1H), 7.77 (s, 1H).	83.5
化合物 38		δ 5.08 (s, 2H), 6.96-7.05 (m, 5H), 7.10-7.20 (m, 5H), 7.26-7.39 (m, 5H), 7.76 (s, 1H).	90.2
化合物 39		δ 2.39 (s, 3H), 5.07 (s, 2H), 7.05 (m, J_{AB} = 8.9Hz, 2H), 7.15-7.32 (m, 8H), 7.76 (s, 1H).	110.6
化合物 40		δ 3.83 (s, 3H), 5.03 (s, 2H), 6.93 (m, J_{AB} = 8.7Hz, 2H), 7.04 (m, J_{AB} = 8.9Hz, 2H), 7.18 (s, 1H), 7.20 (s, 1H), 7.29 (m, J_{AB} = 8.9Hz, 2H), 7.37 (m, J_{AB} = 8.7Hz, 1H), 7.76 (s, 1H).	101.9
化合物 41		δ 5.16 (s, 2H), 7.08 (m, J_{AB} = 8.9Hz, 2H), 7.19 (s, 1H), 7.21 (s, 1H), 7.31 (m, J_{AB} = 8.9Hz, 2H), 7.32-7.65 (m, 9H), 7.77 (s, 1H).	67.0
化合物 42		δ 2.37 (s, 3H), 5.07 (s, 2H), 7.04 (m, J_{AB} = 8.7Hz, 2H), 7.19-7.23 (m, 4H), 7.26-7.35 (m, 4H), 7.76 (s, 1H).	97.3

【0054】
【表7】

化合物 50		δ 3.16 (t, J = 6.8Hz, 2H), 4.21 (t, J = 6.8Hz, 2H), 6.98 (m, J_{AB} = 9.0Hz, 2H), 7.05 (m, 1H), 7.10 (m, 1H), 7.19 (s, 1H), 7.21 (s, 1H), 7.26-7.32 (m, 3H), 7.76 (s, 1H).	108.7
化合物 51		δ 5.15 (s, 2H), 6.89-7.11 (m, 4H), 7.19 (m, 3H), 7.30-7.49 (m, 2H), 7.77 (s, 1H).	102.8
化合物 52		δ 2.05 (m, 2H), 2.41 (t, J = 8.1Hz, 2H), 3.60 (t, J = 7.0Hz, 2H), 3.71 (t, J = 5.2Hz, 2H), 4.15 (t, J = 5.2Hz, 2H), 6.97 (m, J_{AB} = 8.8Hz, 2H), 7.21 (s, 1H), 7.20 (s, 1H), 7.30 (m, J_{AB} = 8.8Hz, 2H), 7.76 (s, 1H).	95.7
化合物 53		δ 5.12 (s, 2H), 7.04 (m, 8.8Hz, 2H), 7.16-7.21 (m, 3H), 7.26-7.39 (m, 4H), 7.77 (s, 1H).	106.6
化合物 54		δ 2.75 (d, J = 2.0Hz, 1H), 5.86 (d, J = 2.0Hz, 1H), 7.17-7.71 (m, 11H), 7.78 (s, 1H).	92.9
化合物 55		δ 0.94 (t, J = 7.2Hz, 6H), 1.26-1.54 (m, 4H), 1.57-1.73 (m, 4H), 4.27 (quint, J = 5.9Hz, 1H), 6.96 (m, J_{AB} = 9.0Hz, 2H), 7.18 (s, 1H), 7.20 (s, 1H), 7.26 (m, J_{AB} = 9.0Hz, 2H), 7.76 (s, 1H).	84.7
化合物 56		δ 2.09-2.15 (m, 2H), 2.14 (s, 3H), 2.71 (t, J = 7.0Hz, 2H), 4.11 (t, J = 6.1Hz, 2H), 6.99 (m, J_{AB} = 8.8Hz, 2H), 7.19 (s, 1H), 7.21 (s, 1H), 7.30 (m, J_{AB} = 8.8Hz, 2H), 7.76 (s, 1H).	95.0

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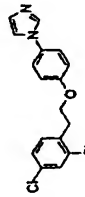
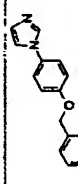
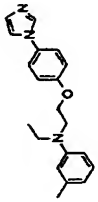
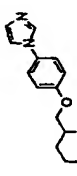
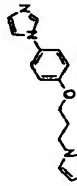
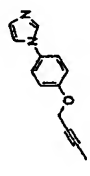
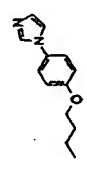
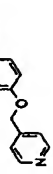
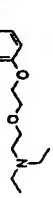
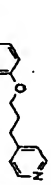
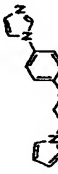
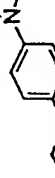
【表９】

化合物 64		δ 3.23 (t, J = 6.7Hz, 2H), 4.21 (t, J = 6.7Hz, 2H), 6.98 (m, J_{AB} = 9.0Hz, 2H), 7.23–7.30 (m, 4H), 7.41 (d, J = 2.2Hz, 1H), 7.76 (s, 1H).	83.2
化合物 65		δ 5.14 (s, 2H), 7.05 (m, J_{AB} = 8.9Hz, 2H), 7.20 (s, 1H), 7.22 (s, 1H), 7.33 (m, J_{AB} = 8.9Hz, 2H), 7.50–7.56 (m, 1H), 7.64–7.70 (m, 2H), 7.77 (s, 1H).	76.9
化合物 66		δ 1.21 (t, J = 7.2Hz, 3H), 2.32 (s, 3H), 3.48 (q, J = 7.2Hz, 2H), 3.74 (t, J = 6.2Hz, 2H), 4.15 (t, J = 6.2Hz, 2H), 6.53–6.67 (m, 3H), 6.97 (m, J_{AB} = 9.0Hz, 2H), 7.10–7.16 (m, 1H), 7.20 (s, 1H), 7.21 (s, 1H), 7.29 (m, J_{AB} = 9.0Hz, 2H), 7.80 (s, 1H).	85.1
化合物 67		δ 1.63–1.82 (m, 6H), 2.40 & 2.43 (m, 3H), 2.60–2.91 (m, 3H), 4.05 & 4.52 (m, 1H), 6.96 (m, 9.0Hz, 2H), 7.19 (d, J = 5.6Hz, 2H), 7.28 (m, J_{AB} = 9.0Hz, 2H), 7.18 (s, 1H), 7.20 (s, 1H), 7.28 (m, J_{AB} = 9.0Hz, 2H), 7.76 (s, 1H).	40.2
化合物 68		δ 2.24 (tt, J = 5.9, 6.7Hz, 2H), 3.91 (t, J = 5.9Hz, 2H), 4.14 (t, J = 6.7Hz, 2H), 6.15 (dd, J = 2.0, 2.2Hz, 2H), 6.66 (dd, J = 2.0, 2.2Hz, 2H), 6.96 (m, J_{AB} = 8.9Hz, 2H), 7.20 (s, 1H), 7.21 (s, 1H), 7.30 (m, J_{AB} = 8.9Hz, 2H), 7.78 (s, 1H).	110.5
化合物 69		δ 1.88 (t, J = 2.2Hz, 3H), 4.70 (q, J = 2.2Hz, 2H), 7.06 (m, J_{AB} = 8.8Hz, 2H), 7.19 (s, 1H), 7.22 (s, 1H), 7.32 (m, J_{AB} = 8.8Hz, 2H), 7.78 (s, 1H). mp 81.0–83.5℃	80.6 7.2
化合物 70		δ 0.99 (t, J = 7.3Hz, 3H), 1.49 (sext, J = 7.3Hz, 2H), 1.73–1.87 (m, 2H), 4.00 (t, J = 6.4Hz, 2H), 6.97 (m, J_{AB} = 8.8Hz, 2H), 7.18 (s, 1H), 7.20 (s, 1H), 7.29 (m, J_{AB} = 8.8Hz, 2H), 7.76 (s, 1H). mp 47.0–50.0℃	98.3

【００５８】
【表１１】

化合物 78		(200 MHz, *DMSO-d_6*) δ 5.26 (s, 2H), 7.09–7.23 (m, 3H), 7.43–7.70 (m, 5H), 8.20 (s, 1H), 8.60 (dd, J = 1.8, 4.6Hz, 2H). mp 104.0–106.0°C	95.1 34.8 94.7 79.0 55.8 110.5 71.8	4.9 62.6 1.1 2.1 106.3 0.8 12.5
化合物 79		δ 1.05 (t, J = 7.2Hz, 6H), 2.62 (q, J = 7.2Hz, 4H), 2.73 (t, J = 6.2Hz, 2H), 3.67 (t, J = 6.2Hz, 2H), 3.84 (m, 2H), 4.16 (m, 2H), 7.01 (m, J_{AB} = 9.0Hz, 2H), 7.18 (s, 1H), 7.20 (s, 1H), 7.29 (m, J_{AB} = 9.0Hz, 2H), 7.76 (s, 1H).		
化合物 80		δ 2.16 (ddt, J = 6.2, 7.3, 8.1Hz, 2H), 2.85 (dd, J = 7.3, 8.1Hz, 2H), 4.00 (t, J = 6.2Hz, 2H), 6.97 (m, J_{AB} = 8.9Hz, 2H), 7.15–7.22 (m, 4H), 7.30 (m, J_{AB} = 8.9Hz, 2H), 7.77 (s, 1H), 8.51–8.54 (m, 2H). mp 70.0–72.0°C		
化合物 81		δ 2.28 (ddt, J = 6.2, 7.0, 8.1Hz, 2H), 3.01 (dd, J = 7.0, 8.1Hz, 2H), 4.05 (t, J = 6.2Hz, 2H), 6.97 (m, J_{AB} = 9.0Hz, 2H), 7.11–7.21 (m, 4H), 7.30 (m, J_{AB} = 9.0Hz, 2H), 7.61 (dt, J = 1.8, 7.5Hz, 1H), 7.76 (s, 1H), 8.56 (d, J = 4.0Hz, 1H). mp 64.0–66.0°C		
化合物 82		δ 1.01 (s, 6H), 2.29 (s, 6H), 2.30 (s, 2H), 3.74 (s, 2H), 7.01 (m, J_{AB} = 8.8Hz, 2H), 7.19 (s, 1H), 7.20 (s, 1H), 7.29 (m, J_{AB} = 8.8Hz, 2H), 7.76 (s, 1H). mp 84.0–86.0°C		
化合物 83		(200 MHz, *DMSO-d_6*) δ 4.27 (s, 4H), 6.00 (t, J = 2.2Hz, 2H), 6.85 (t, J = 2.2Hz, 2H), 7.00–7.13 (m, 3H), 7.49–7.60 (m, 2H), 7.64 (t, J = 1.3Hz, 1H), 8.13 (t, J = 1.1Hz, 1H). mp 128.5–129.0°C		
化合物 84	 TsOH	*DMSO-d_6*, δ 0.36 (m, 2H), 0.60 (m, 2H), 1.25 (m, 1H), 2.29 (s, 3H), 3.91 (d, J = 7.0Hz, 2H), 7.10–7.21 (m, 4H), 7.49 (m, J_{AB} = 7.9Hz, 2H), 7.71 (m, J_{AB} = 9.2Hz, 2H), 7.90 (dd, J = 1.3, 1.9Hz, 1H), 8.22 (dd, J = 1.5, 1.9Hz, 1H), 9.60 (dd, J = 1.3, 1.5Hz, 1H). mp 136.0–138.0°C		

【００６０】
【表１３】

化合物 91		(200 MHz, *DMSO-d_6*) δ 0.98 (s, 9H), 1.68 (t, *J* = 7.0Hz, 2H), 2.29 (s, 3H), 4.11 (t, *J* = 7.0Hz, 2H), 7.11 (m, J_{AB} = 7.9Hz, 2H), 7.19 (m, J_{AB} = 9.0Hz, 2H), 7.48 (m, J_{AB} = 8.1Hz, 2H), 7.71 (m, J_{AB} = 9.0Hz, 2H), 7.90 (dd, *J* = 1.5, 1.8Hz, 1H), 8.21 (dd, *J* = 1.3, 1.8Hz, 1H), 9.58 (dd, *J* = 1.3, 1.5Hz, 1H). mp 220.0-221.0℃	101.8	1.8
化合物 92		*DMSO-d_6*, δ 0.95 (d, *J* = 6.4Hz, 6H), 1.64 (q, *J* = 6.4Hz, 2H), 1.80 (m, 1H), 2.29 (s, 3H), 4.08 (t, *J* = 6.4Hz, 2H), 7.12 (m, J_{AB} = 7.9Hz, 2H), 7.18 (m, J_{AB} = 9.0Hz, 2H), 7.49 (m, J_{AB} =7.9Hz, 2H), 7.71 (m, J_{AB} = 9.0Hz, 2H), 7.90 (dd, *J* = 1.3, 1.9Hz, 1H), 8.21 (dd, *J* = 1.5, 1.9Hz, 1H), 9.59 (dd, *J* = 1.3, 1.5Hz, 1H). mp 187.0-189.0℃	102.8	2.3
化合物 93		(200 MHz, *DMSO-d_6*) δ 0.93 (d, *J* = 6.2Hz, 3H), 1.08-2.10 (m, 13H), 2.29 (s, 3H), 4.09 (t, *J* = 7.0Hz, 2H), 5.10 (m, 1H), 7.08-7.25 (m, 4H), 7.48 (m, J_{AB} = 8.1Hz, 2H), 7.71 (m, J_{AB} = 9.0Hz, 2H), 7.90 (dd, *J* = 1.3, 2.0Hz, 1H), 8.21 (dd, *J* = 1.5, 2.0Hz, 1H), 9.58 (dd, *J* = 1.3, 1.5Hz, 1H). mp 152.0-153.0℃	100.2	5.3
化合物 94		*DMSO-d_6*, δ 0.99 (t, *J* = 7.5Hz 3H), 1.76 (tq, *J* = 6.6, 7.5Hz, 2H), 2.29 (s, 3H), 4.02 (t, *J* = 6.6Hz, 2H), 7.12 (m, J_{AB} = 7.9Hz, 2H), 7.17 (m, J_{AB} = 9.0Hz, 2H), 7.49 (m, J_{AB} =7.9Hz, 2H), 7.72 (m, J_{AB} = 9.0Hz, 2H), 7.90 (dd, *J* = 1.3, 1.9Hz, 1H), 8.22 (dd, *J* = 1.5, 1.9Hz, 1H), 9.61 (dd, *J* = 1.3, 1.5Hz, 1H). mp 148.0-150.0℃	82.7	7.7
化合物 95		(200 MHz, *DMSO-d_6*) δ 1.11 (t, *J* = 7.0Hz, 3H), 1.90-2.05 (m, 2H), 2.29 (s, 3H), 3.44 (q, *J* = 7.0Hz, 2H), 3.52 (t, *J* = 6.2Hz, 2H), 4.11 (t, *J* = 8.4Hz, 2H), 7.11 (m, J_{AB} = 8.3Hz, 2H), 7.19 (m, J_{AB} = 9.2Hz, 2H), 7.48 (m, J_{AB} = 8.1Hz, 2H), 7.71 (m, J_{AB} = 9.0Hz, 2H), 7.89 (dd, *J* = 1.5, 1.8Hz, 1H), 8.21 (dd, *J* = 1.3, 1.8Hz, 1H), 9.56 (dd, *J* = 1.3, 1.5Hz, 1H). mp 122.5-124.0℃	94.3	2.0
化合物 96		*DMSO-d_6*, δ 1.77 (t, *J* = 2.6Hz, 3H), 2.29 (s, 3H), 2.58-2.66 (m, 2H), 4.12 (t, *J* = 6.7Hz, 2H), 7.11 (d, *J*= 7.7Hz 2H), 7.20 (m, J_{AB} = 9.0Hz, 2H), 7.48 (m, J_{AB} = 8.1Hz, 2H), 7.72 (m, J_{AB}= 9.0Hz, 2H), 7.89 (t, *J* = 1.5, 1.8Hz, 1H), 8.22 (t, *J* = 1.3, 1.8Hz, 1H), 9.58 (t, *J* = 1.3, 1.5Hz, 1H). mp 147.5-149.5℃	95.8	5.0

【0062】
【表15】

化合物103		δ 1.03 (t, J = 7.5 Hz, 3H), 1.76-1.83 (m, 2H), 2.34 (s, 3H), 2.98 (t, J = 7.3 Hz, 2H), 7.29 (dd, J = 1.3, 1.6Hz, 1H), 7.53 (d, J = 8.2Hz, 1H), 7.66 (dd, J = 1.5, 1.6Hz, 1H), 7.97 (dd, J = 1.9, 8.2Hz, 1H), 8.00 (d, J = 1.9Hz, 1H), 9.35 (dd, J = 1.3, 1.5Hz, 1H). mp 199.5-201.0℃		
化合物104		(200 MHz) δ 1.30 (t, J = 7.5 Hz, 3H), 2.78 (q, J = 7.5 Hz, 2H), 7.40-7.50 (m, 5H), 7.58 (d, J = 1.3Hz, 1H), 9.05 (s, 1H).		
化合物105		(200 MHz) δ 0.89 (t, J = 6.8 Hz, 3H), 1.13-1.43 (m, 8H), 1.50-1.75 (m, 2H), 2.70 (t, J = 7.3 Hz, 2H), 7.35-7.65 (m, 6H), 9.35 (dd, J = 1.3, 1.5Hz, 1H).		
化合物106		(200 MHz) δ 1.28 (s, 3H), 1.31 (s, 3H), 3.02 (m, 1H), 7.40-7.63 (m, 6H), 9.43 (dd, J = 1.3, 1.5Hz, 1H). mp 205.5-207.5℃		
化合物107		(200 MHz) δ 0.85 (t, J = 7.5 Hz, 3H), 1.28 (d, J = 6.8Hz, 3H), 1.55-1.75 (m, 2H), 2.63-2.84 (m, 2H), 7.38-7.53 (m, 5H), 7.59 (dd, J = 1.3, 1.8Hz, 1H), 9.13 (dd, J = 1.3, 1.5Hz, 1H). mp 142.0-146.0℃		
化合物108		(200 MHz) δ 0.97 (t, J = 7.3Hz, 3H), 1.58-1.80 (m, 2H), 2.69 (t, J = 7.3Hz, 2H), 7.35-7.55 (m, 5H), 7.59 (dd, J = 1.3, 1.8Hz, 1H), 9.29 (dd, J = 1.3, 1.5Hz, 1H). mp 155.5-157.0℃		
化合物109		*DMSO-d_6*, δ 2.29 (s, 6H), 2.29 (s, 6H), 2.83 (s, 3H), 2.85 (s, 3H), 3.24 (m, 2H), 4.13 (t, J = 6.0Hz, 2H), 7.12 (m, J_{AB} = 8.0Hz, 4H), 7.18 (m, J_{AB} = 9.0Hz, 2H), 7.49 (m, J_{AB} = 8.0Hz, 4H), 7.74 (m, J_{AB} = 9.0Hz, 2H), 7.92 (dd, J = 1.3, 1.9Hz, 1H), 8.22 (dd, J = 1.5, 1.9Hz, 1H), 9.61 (dd, J = 1.3, 1.5Hz, 1H). mp 95.0-98.0℃	35.9	50.6

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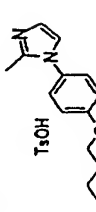
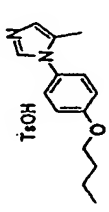
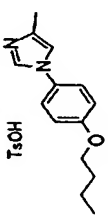
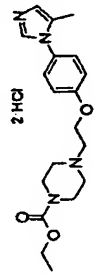
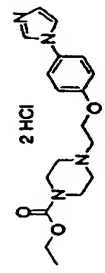
【表１７】

化合物117		*DMSO-d_6*, δ 1.00 (t, J = 7.3Hz, 3H), 1.52 (m, 2H), 1.83 (m, 2H), 2.37 (s, 3H), 2.68 (s, 3H), 4.04 (t, J = 6.4Hz, 2H), 7.18-7.27 (m, 4H), 7.42 (s, 1H), 7.88 (m, J_{AB} = 8.1Hz, 2H). mp 148.0-149.0℃	>300.0
化合物118		*DMSO-d_6*, δ 0.95 (t, J = 7.3Hz, 3H), 1.45 (tq, J = 7.3, 7.7Hz, 2H), 1.67-1.80 (m, 2H), 2.17 (d, J = 0.9Hz, 3H), 2.29 (s, 3H), 4.07 (t, J = 6.5Hz, 2H), 7.09-7.21 (m, 4H), 7.48 (m, J_{AB} = 8.1Hz, 2H), 7.55 (m, J_{AB} = 8.8Hz, 2H), 9.25 (d, J = 1.5Hz, 1H). mp 163.0-164.0℃	3.4
化合物119		δ 0.99 (t, J = 7.3Hz, 3H), 1.45 (tq, J = 7.3, 7.7Hz, 2H), 1.72-1.83 (m, 2H), 2.17 (d, J = 0.9Hz, 3H), 3.99 (t, J = 6.5Hz, 2H), 6.92-7.00 (m, 1H), 6.96 (m, J_{AB} = 9.0Hz, 2H), 7.26 (m, J_{AB} = 9.0Hz, 2H), 7.66 s, 1H). mp 130.0-130.5℃	173.1
化合物120		*DMSO-d_6*, δ 1.21 (t, J = 7.0Hz, 3H), 2.17 (s, 3H), 3.11-3.50 (m, 8H), 3.55 (t, J = 4.8Hz, 2H), 4.09 (q, J = 7.0Hz, 2H), 4.52 (t, J = 4.8Hz, 2H), 7.25 (m, J_{AB} = 9.0Hz, 2H), 7.56-7.64 (m, 3H), 9.26 (s, 1H). mp 212.0-214.5℃	56.5
化合物121		*DMSO-d_6*, δ 1.21 (t, J = 7.2Hz, 3H), 3.00-3.83 (m, 8H), 3.56 (t, J = 4.8Hz, 2H), 4.09 (q, J = 7.2Hz, 2H), 4.54 (t, J = 4.7Hz, 2H), 7.28 (m, J_{AB} = 9.0Hz, 2H), 7.78 (m, J_{AB} = 9.0Hz, 2H), 7.89 (dd, J = 1.4, 1.9Hz, 1H), 8.21 (dd, J = 1.4, 1.9Hz, 1H), 9.64 (t, J = 1.4Hz, 1H). mp 199.5-202.0℃	16.2

【００６６】

試験例［ヒト腎ミクロソーム由来２０－ＨＥＴＥ産生酵素の阻害作用］

上記表記載の化合物について、２０－ＨＥＴＥ産生阻害作用を試験した。

本試験はＪ．Ｐｈａｒｍａｃｏｌ．Ｅｘｐ．Ｔｈｅｒ．，第２６８巻，第４７４頁（１９９４）に記載の方法に準拠して行った。

ＤＭＳＯで１μＭに調製した被験薬溶液を、５ｍＭの塩化マグネシウム及び１ｍＭのエチ

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A61P 9/10	A61P 9/10	
A61P 13/12	A61P 13/12	
A61P 43/00	A61P 43/00	111
C07D 401/12	C07D 401/12	
C07D 403/12	C07D 403/12	
C07D 405/12	C07D 405/12	
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(72)発明者 中村 年男
東京都豊島区高田３丁目２４番１号 大正製薬株式会社内

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